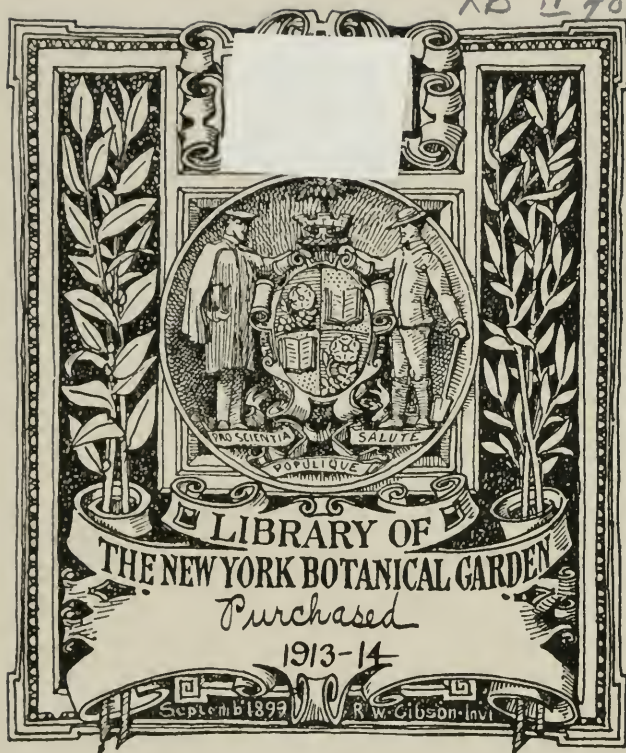


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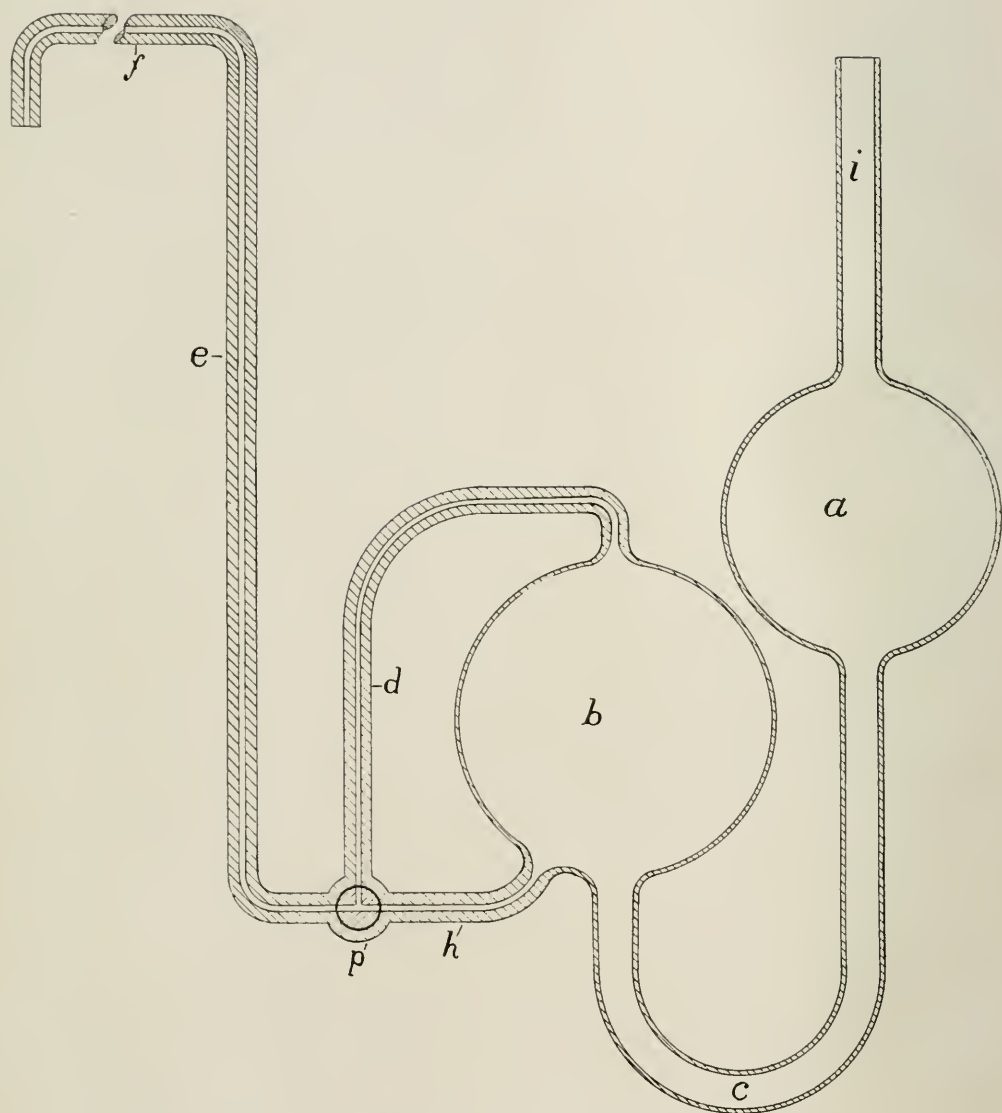
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BENEDICT: A MODIFIED HEMPEL GAS PIPETTE.

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## A MODIFIED HEMPEL GAS PIPETTE

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(WITH PLATE I)

In the use of the Hempel pipette the shaking necessary to obtain complete absorption of a gas is undesirable from two standpoints. It is time-consuming and, unless the connections are exactly right, air is apt to enter the apparatus during the protracted period of vigorous shaking which is often necessary.

Van Slyke, in his latest apparatus for amino nitrogen determination, employs a small motor for shaking the pipette, and thus obviates the awkward procedure of shaking by hand.

The modified form of apparatus here described was designed to eliminate entirely any necessity for shaking in the Hempel apparatus to secure complete absorption. The figure is almost self-explanatory (Plate I). At *p* is a three-way stop-cock, through which the gas is allowed to enter *b* through the tube *h*. The gas thus bubbles through the solution contained in *b*, collects at the top, and is drawn out through the tube *d*, after turning *p*. The intimate mixture of gas and liquid effected by bubbling the gas through the solution is sufficient to ensure a complete reaction if the process is repeated once or twice. We have used the apparatus in this laboratory in a large number of determinations, with highly satisfactory results.

# THE INFLUENCE OF ARSENIC UPON THE BIOLOGICAL TRANSFORMATION OF NITROGEN IN SOILS

J. E. GREAVES

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Arsenic occurs in many virgin soils and is repeatedly added to others in insecticides, in commercial fertilizers, or in the flue dust from various smelters. Some investigators hold that arsenic may accumulate in soil in quantities sufficient to injure vegetation grown upon such soil, and that the plants may in turn poison animals which feed upon them. The work described in this paper was undertaken to see if the lower plants, the ammonifiers and nitrifiers, of the soil are injured by arsenic, for they are readily experimented with and yield results in much shorter time than higher plants. Such results may also indicate the way in which a study of the higher plants should be pursued, for it is probable that substances which influence the soil organisms may also influence higher plants, differing only in degree; but results of this kind must be accepted only as indicative, not as absolute proof, of what may occur with higher plants, for as pointed out by Guthrie and Helms,<sup>1</sup> all plants are not equally sensitive to poisons.

## I. INFLUENCE OF ARSENIC UPON AMMONIFICATION

**Method of experimentation.** The work was carried on with a typical bench soil, a sandy loam, fairly high in calcium and iron content, and supplied with an abundance of all the essential elements of plant food with the exception of nitrogen which was low, a characteristic of arid soils. The soil was air dried, sieved and stored in a large box, so that all determinations could be made on the same soil.

Determination of the ammonifying powers was made by Lip-

<sup>1</sup> Guthrie and Helms: *Agr. Gaz. New South Wales*, 1903, xiv, p. 114.

man's<sup>2</sup> method, with slight modifications. Beakers covered with Petri dishes were sterilized and into these were weighed 100-gm. portions of the air dried soil and 1 gm. of dry blood. Sodium arsenate was added from a standard solution with the proper proportion of sterile water. The dry insoluble compounds were thoroughly mixed with the soil and then the water content of the soil made up to 18 percent with distilled sterile water. The samples were incubated at 28° C. to 30° C. for four days and the ammonia determined by transferring to Kjeldahl flasks with 250 cc. of distilled water, adding 2 grams of magnesium oxide and distilling into *n*/10 sulfuric acid sol. The determinations were made in duplicate and compared with sterile blanks, so that each reported result is the average of two or more closely agreeing determinations. The results for soluble arsenic (sodium arsenate) are given in Table 1.

TABLE I

*Data pertaining to the ammonia produced in 100 grams of soil containing different amounts of arsenic in the form of sodium arsenate*

Arsenic; parts per million	Milligrams of NH <sub>3</sub> formed	Arsenic; parts per million	Milligrams of NH <sub>3</sub> formed	Arsenic; parts per million	Milligrams of NH <sub>3</sub> formed
None	48.02	.....	.....	.....	.....
1	48.24	10	45.06	55	32.12
2	52.72	15	45.06	60	32.78
3	58.12	20	36.54	65	34.82
4	53.36	25	38.90	70	34.00
5	52.68	30	38.22	75	34.40
6	51.02	35	36.00	80	32.12
7	51.66	40	32.78	85	32.68
8	46.76	45	34.80	90	33.60
9	46.76	50	32.60	.....	.....

From the above results it may be seen that, in dilute solution, sodium arsenate stimulated the activity of the ammonifying organisms of the soil, the greatest influence having been exerted at a concentration of 3 parts per million. The effect was quite marked up to a concentration of 7 parts per million. Part of this stimulating action, however, may have been due to the anion and not to the cation, as Lipman in his work has noted a stimulating effect with some sodium compounds. No retarding influence was noted until the concentration of the sodium arsenate reached 20 parts per million,

<sup>2</sup> Lipman: *Centralbl. f. Bakteriologie*, 1912, xxxii, p. 8.

after which there was a marked retarding influence on the ammonifying powers of the soil. From this point the quantity of ammonia formed was nearly constant; only a slightly greater retarding effect having been noted when the concentration of the arsenic was 90 parts per million than when it was 20. This is probably due to the fact that the soil was comparatively rich in calcium and iron, and that the sodium arsenate was changed into the comparatively insoluble calcium and iron arsenates. At the concentration of 20 parts per million the water in the soil was saturated with these slightly soluble compounds, so that even though there was an increase in the quantities added, the active masses remained about constant. These results, therefore, cannot be taken to indicate what may happen in a soil devoid of calcium and iron, and in which the arsenic may remain in a soluble form. They show that large quantities of soluble arsenic, even up to 90 parts per million, may be added to a soil rich in calcium and iron without stopping ammonification.

**The influence of insoluble arsenic compounds.** The compounds selected for the tests are in use as sprays, and hence find their way into the soil in greater or less quantities. They were lead arsenate, Paris green, zinc arsenite and arsenic trisulfide. The trisulfide, while seldom used, is of special interest in this work in that it permits the application of arsenic free from the metallic elements which accompany each of the others, and therefore gives more nearly the influence of the arsenic than do the other compounds. In each case the quantity of the compound taken was such as to give equivalent amounts of arsenic. The results reported are in milligrams of ammonia formed per 100 grams of soil. These results are reported in Table 2.

On examining the data in Table 2 we find that *arsenate* stimulated ammonification in the lowest concentrations and that the toxicity gradually increased as the amount of lead arsenate in the soil was increased. For no concentration tested was there any marked retarding action over the previous concentration, but a gradual decline in the ammonifying efficiency. The ammonia was not reduced to one-half of its original amount until the soil contained a concentration of 760 parts of arsenic per million. Even at a concentration of 1,120 parts per million of arsenic, there was produced

TABLE 2

*Data pertaining to the ammonia produced in 100 grams of soil containing different amounts, and different forms, of arsenic*

Arsenic added ; parts per million	Lead arsenate ; milligrams NH <sub>3</sub> formed	Paris green ; milligrams NH <sub>3</sub> formed	Zinc arsenite ; milligrams NH <sub>3</sub> formed	Arsenic trisulfide ; milligrams NH <sub>3</sub> formed
None	40.46	39.28	34.25	39.44
20	41.82	32.64	35.02	43.46
40	38.42	28.22	33.32	46.92
80	38.41	26.52	28.22	42.16
120	35.02	26.86	24.82	42.16
160	35.36	20.74	22.44	40.80
200	35.70	21.42	21.12	39.78
240	36.72	19.72	18.02	40.13
280	33.32	19.38	17.34	41.08
320	33.66	19.38	17.34	40.44
360	28.22	15.98	17.00	40.80
400	27.28	15.30	17.80	40.46
440	27.20	13.94	17.34	40.79
480	28.80	10.20	17.00	39.79
520	25.16	10.54	17.34	40.11
560	24.34	6.12	17.68	38.77
600	24.34	4.42	18.02	40.12
640	23.46	5.10	18.02	39.77
680	22.78	4.42	17.68	39.44
720	21.76	5.10	17.85	38.41
760	20.40	4.42	17.68	38.75
800	20.00	4.42	17.51	39.10
840	20.40	4.42	17.51	38.41
880	20.40	4.42	17.68	38.72
920	20.40	4.76	17.68	38.08
960	19.09	4.42	17.34	37.74
1,000	19.04	4.76	15.64	37.40
1,040	18.36	3.16	15.64	36.71
1,080	19.02	2.72	15.81	36.70
1,120	15.20	0.68	15.30	36.38

over one-third of the amount of ammonia formed in the total absence of lead arsenate, showing that even this large quantity was not sufficient to kill or even to entirely stop the activity of the soil organisms.

*Paris green*, on the other hand, acts as a strong poison to the ammonifying organisms. Before the concentration of arsenic in this form in the soil reached a concentration of 240 parts per million, the ammonifying efficiency of the soil was reduced one-half. Even 20 parts per million of arsenic retarded very materially the ammonifying powers of the soil. At the highest concentration tested (1,120 parts per million) practically no ammonia was formed.

*Arsenic trisulfide* in the lowest concentration had a marked



stimulating effect on ammonification and no toxic influence was noted until the highest proportions were present. Even 1,120 parts of arsenic per million exerted little toxic influence.

The *zinc arsenite* and *lead arsenate* are very similar in their action, for they both apparently stimulate the ammonifying organisms of the soil when used in small quantities; and while in greater concentration they exert a certain toxic influence upon the soil organisms, this influence increases slowly with the added quantity of the salt. The power of the soil to produce ammonia, after 800 parts of arsenic in the form of lead arsenate had been added, was 49.43 percent of the power of the original soil, while with the same arsenic concentration in the form of zinc arsenite, it was reduced to 51.11 percent. At the highest concentration tested, 1,120 parts per million, the lead arsenate reduced the ammonifying efficiency to 37.57 percent of the original soil while the zinc arsenite reduced it to 44.68 percent of the original soil. Furthermore, it may be seen that neither of these salts retarded very materially the ammonifying powers of the soil when present in a quantity equal to that known to occur in soils.<sup>2a</sup> This, however, is not the case when the arsenic is applied in the form of Paris green. This substance, even in the lowest concentration, retards very materially the ammonifying powers of the soil.

## II. INFLUENCE OF ARSENIC UPON NITRIFICATION

**Method of experimentation.** Soil similar to that used in the ammonification tests was employed. The method was that of Lipman.<sup>2b</sup> Beakers covered with Petri dishes were sterilized and into these were weighed 100-gm. portions of the air-dried soil and 2 gm. of dry blood. Sodium arsenate was added from a standard solution with the proper proportion of sterile water, and the mixture thoroughly stirred with a sterile spatula. The so-called insoluble arsenates were added in the form of the dry powders and then thoroughly mixed with a sterile spatula. Sufficient sterile distilled water was added to make the moisture content of the soil 18 percent. These portions were weighed and the moisture content made up weekly to 18 percent.

<sup>2a</sup> Greaves: *BIOCHEMICAL BULLETIN*, 1913, ii, p. 519.

<sup>2b</sup> Lipman: *Centralbl. f. Bakteriol.*, 1912, xxxii, p. 8.



The mixtures were incubated at 28° C. to 30° C. for three weeks and the nitrates determined by transferring the soil, by means of 250 c.c. of distilled water, to a mortar containing 2 gm. of quick lime. The soil was triturated for 2 minutes and then transferred to a closed bottle and allowed to stand for 12 hours. At the end of this time an aliquot portion, 25 c.c., was measured into a 100 c.c. beaker and evaporated to dryness. The residue was treated with 2 c.c. of phenol-disulphonic acid equally distributed over all the residue and then allowed to stand for 10 minutes. The resulting solution was diluted with water and the excess of acid neutralized with dil. ammonium hydroxid sol. The ensuing color was compared with that produced by a standard solution of potassium nitrate treated in the same manner. The determinations were all made in duplicate and compared with sterile blanks, so that each reported result is the average of two or more closely agreeing determinations. The results obtained for soluble arsenic (sodium arsenate) are given in Table 3.

TABLE 3

*Data pertaining to nitric nitrogen produced in 100 grams of soil containing different amounts of arsenic in the form of sodium arsenate*

Arsenic; parts per million	Milligrams of nitric nitrogen formed	Arsenic; parts per million	Milligrams of nitric nitrogen formed	Arsenic; parts per million	Milligrams of nitric nitrogen formed
None	9.7	10	9.5	55	9.8
1	9.6	15	9.2	60	9.6
2	9.6	20	9.8	65	9.7
3	9.4	25	10.4	70	9.5
4	9.0	30	10.3	75	11.1
5	9.2	35	9.0	80	14.5
6	9.8	40	9.0	85	15.6
7	9.5	45	9.0	90	9.4
8	10.2	50	9.6	100	6.0
9	9.8	.....	.....	.....	.....

A striking general similarity is seen to exist between the results here presented and those found for the ammonification series. No toxicity was noted until 100 parts per million were present. It is likely that the main part of the soluble arsenic was transformed into the comparatively insoluble iron and calcium arsenates, hence the great similarity throughout the entire series. The stimulation caused when the concentration was from 75 to 85 parts per million

was probably due partly to the sodium ion. As Lipman<sup>3</sup> has noted, there is a marked stimulation of nitrification in soils when small quantities of either sodium sulphate or sodium chloride are applied to them.

TABLE 4

*Data pertaining to nitric nitrogen produced in 100 grams of soil containing different amounts, and different forms, of arsenic*

Arsenic added ; parts per million	Lead arsenate ; milligrams of nitric nitrogen formed	Paris green ; milligrams of nitric nitrogen formed	Zinc arsenite ; milligrams of nitric nitrogen formed	Arsenic trisulfide ; milligrams of nitric nitrogen formed
None	10.5	10.4	10.2	9.5
20	17.9	10.8	10.5	10.2
40	18.7	9.4	10.8	11.3
80	14.5	9.6	10.0	13.2
120	13.5	10.0	9.8	11.3
160	13.5	9.7	10.3	11.9
200	12.5	9.9	9.3	10.2
240	11.5	10.4	10.3	10.2
280	9.5	13.4	9.7	11.6
320	10.2	15.4	9.4	9.7
360	10.3	14.4	9.9	9.2
400	9.8	13.4	10.8	9.6
440	9.7	14.0	9.0	10.0
480	9.6	14.1	14.0	8.8
520	10.5	13.4	14.4	8.3
600	10.3	13.4	15.0	6.3
640	10.0	12.4	16.8	5.4
680	9.8	10.4	12.1	6.5
720	9.5	11.0	10.0	5.0
760	9.4	9.9	9.0	4.0
800	9.3	9.7	8.6	4.0
840	8.5	9.4	7.4	3.9
880	8.4	9.4	6.8	2.2
920	8.2	9.4	6.0	2.2
960	8.0	8.4	6.8	2.0
1,000	7.9	7.4	7.0	1.0
1,040	7.8	7.4	6.0	1.0
1,080	7.5	5.4	5.2	1.0
1,120	7.1	3.4	5.3	0.8

**The influence of insoluble arsenic compounds.** The compounds used in the ammonification tests were employed for this series : lead arsenate, Paris green, zinc arsenite and arsenic trisulfide. In each case the quantity of the compound taken was such as to give equivalent amounts of arsenic. The results, reported as milligrams of nitric nitrogen per 100 grams of soil, are given in Table 4.

These results bring out some very interesting facts, which are

<sup>3</sup> Lipman : *Centralbl. f. Bakteriöl.*, 1912, xxxii, p. 8.

of considerable theoretical and practical importance. We note a marked stimulating effect with each of the substances used, which varied greatly with the different compounds. For instance, there was great stimulation with *lead arsenate* in the lowest concentration tested. At this concentration the quantity of resultant nitric nitrogen was nearly twice that produced in the untreated soil. As the concentration of the arsenic increased above 240 parts per million there was a slight decrease in the production of nitric nitrogen, but a concentration of even 1,120 parts of arsenic in the form of lead arsenate caused the production of nearly as much nitric nitrogen as was formed in the untreated soil. It is rather hard to decide, from these results, whether the observed stimulation was due to the chemical applied or to a change in the physical condition of the soil. Probably both are concerned but only a small portion can be attributed to a purely physical change in the soil.

Examining the results obtained where the *Paris green* was used, we find a stimulating effect with the lower concentrations of arsenic, which reached its maximum when 320 parts per million of arsenic were present. Above this concentration it decreased and at a concentration of 760 parts per million of arsenic the effect commenced to be toxic. The toxicity increased with the concentration until, at the highest concentrations, the production of nitric nitrogen was reduced to 3.4 mg. of nitric nitrogen per 100 gm. of soil.

*Zinc arsenite* exerted no apparent influence on the formation of nitric nitrogen in the soil until the concentration was 480 parts per million; after which a notable stimulating influence was observed. This stimulation continued until the concentration was 680 parts per million. Above this concentration there was a marked retarding influence upon nitrification.

*Arsenic trisulfide* stimulated the formation of nitric nitrogen slightly until the concentration of the arsenic trisulfide exceeded 280 parts per million; after which there was a marked falling off in the production of nitric nitrogen and at the highest concentration tested (1,120 parts per million), the formation of nitric nitrogen practically ceased.

Paris green, zinc arsenite and arsenic trisulfide after their first slight stimulating influence, which varied in intensity with the dif-

ferent compounds, exerted very marked toxic influences. This was greatest for arsenic trisulfide and least for zinc arsenite. It is improbable that sufficiently large quantities of any of these compounds (lead arsenate, zinc arsenite, arsenic trisulfide, Paris green), would be added to a soil under natural systems of agriculture to very materially retard nitrification. On the other hand, these results indicate that a marked stimulating influence may be exerted.

### III. GENERAL CONSIDERATIONS

Throughout this work there has been noted a wide difference in the quantitative action of arsenic compounds, but a striking similarity in qualitative influence. Some exerted little influence in the lowest concentrations on either ammonification or nitrification, but in the higher concentrations exerted a very marked toxic influence, *e. g.*, Paris green. All, at some concentration, exerted either a slight or very great stimulating influence. This fact suggests that arsenic in small quantities tends to stimulate the bacterial activity of the soil as measured by ammonification and nitrification. On the other hand, the absence of any great toxic influence where the soluble arsenic was applied and the great variations in results noted with other compounds, raise the question whether the toxic influence is exerted by the anion or cation.

In order to gain some light on this subject, determinations were made of the water-soluble arsenic in soil to which the various forms of arsenic were added. These determinations were made as follows: Quantities of *lead arsenate*, *Paris green*, *zinc arsenite*, and *arsenic trisulfide* were added to 100-gm. portions of soil in quantities sufficient to give 1,120 parts of arsenic per million of soil. The soil and arsenic, together with 2 gm. of dry blood, were placed in sterile tumblers; the water content was made up to 18 percent and then incubated at 28° C. for three weeks. At the end of this time the soil was transferred by means of 1,000 c.c. of carbon dioxide-free, distilled water to large acid bottles. The mixture was left in these bottles with occasional shaking for eight days, then filtered, and the arsenic determined<sup>4</sup> in an aliquot part. In another set the various forms of arsenic were mixed with 100-gm. portions of soil

<sup>4</sup> Greaves: *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 150.

and 2 gm. of dry blood, and the water-soluble arsenic determined as above, without incubating. The average of the two sets of results should give a very close approximation of the quantity of water-soluble arsenic existing in the soil during the activity of the organisms.

The results are given in Table 5, as milligrams of water-soluble arsenic occurring in 100 gm. of the soil (before and after three weeks' incubation), to which 1,120 parts per million of the various forms of arsenic were added. Each is the average of two or more closely agreeing determinations.

TABLE 5

*Data pertaining to water-soluble arsenic in 100 grams of soil to which 1120 parts per million of arsenic were added*

Treatment	Lead arsenate	Paris green	Zinc arse- nite	Arsenic trisulfide
Incubated three weeks. Water-soluble arsenic determined (mg.).....	14.3	80.0	36.9	50.0
Water-soluble arsenic determined directly (mg.).....	20.2	82.0	31.7	5.6
Average (mg.).....	17.3	81.0	34.3	27.3

These results show that there are great differences in the quantities of water-soluble arsenic in a soil to which various forms of arsenic have been added, and that even soil rich in iron and calcium to which arsenic has been added in large quantities may have a high water-soluble arsenic content. This content is highest when the arsenic is added in the form of *Paris green*. *Paris green* apparently becomes less soluble, while arsenic trisulfide becomes much more soluble, as nitrification takes place. Comparing these results with the ammonia and nitrates formed under the several conditions, we note a general relationship between the toxicity of the substance added and the quantity of water-soluble arsenic present. The greatest toxic effect is noted with *Paris green* and this gives the greatest amount of water-soluble arsenic.

Part of this toxicity may be due to the copper ion, as it is well known that this substance acts as a strong poison to many of the lower plants. Miss Benchley<sup>5</sup> found it to be toxic to higher plants

<sup>5</sup> Benchley: *Annals of Botany*, 1910, xxiv, p. 571.



also, when present to the extent of only 1 part per ten million of water. Although Russell<sup>6</sup> states that it is not as toxic in soil as in water, he and Darkshire<sup>7</sup> found it to be toxic in soils; and they failed to get a stimulating influence with it. Montemartini<sup>8</sup> has noted a stimulation with copper sulphate when used in dilute solutions. This, however, may have been due to the anion and not to the cation, as sulphates do stimulate plant growth by their action on insoluble constituents of the soil.<sup>9</sup> Clark and Gage<sup>10</sup> have found that very dilute solutions of copper have an invigorating influence upon bacterial activity. In order that any stimulation may be noted, the copper must be present in very small quantities. Jackson<sup>11</sup> found that 1 part of copper sulphate in 50,000 parts of water killed *B. coli* and *B. typhosus*. Kellerman and Beckwith<sup>12</sup> found that the common saprophytic bacteria are more resistant to copper than is *B. coli*; their results also show stimulating influences at some concentrations. So it is likely that both the copper and arsenic stimulated in these experiments.

With all the other compounds tested there was either a marked or very slight stimulation. This is in keeping with the findings of other investigators. Johnson<sup>13</sup> found that arsenic, in dilute solutions, stimulated seeds, while Bouilhac<sup>14</sup> found that it stimulated algae. Stimulation of nitrification may be due either to the arsenic inhibiting or killing injurious species, or to a direct stimulation. It seems remarkable that bacteria should function in the presence of the large quantities of water-soluble arsenic which were present in some of these tests. One would be prone to ascribe the nitrification to something other than a biological influence, were it not for the fact that Gosio<sup>15</sup> grew moulds in organic matter containing

<sup>6</sup> Russell: *Soil Conditions and Plant Growth*; New York and London, 1912, p. 47.

<sup>7</sup> Russell and Darkshire: *Jour. Agr. Sci.*, 1905, i, p. 261.

<sup>8</sup> Montemartini: *Bull. Agr. Bur. Intel. and Plant Diseases*, 1911, ii, p. 2467.

<sup>9</sup> Greaves: *Jour. Biological Chem.*, 1910, vii, p. 298.

<sup>10</sup> Clark and Gage: *Jour. Infect. Diseases*, 1906, ii, p. 175.

<sup>11</sup> Jackson: *Jour. Amer. Chem. Soc.*, 1905, xxvii, p. 675.

<sup>12</sup> Kellerman and Beckwith: *U. S. Dep. Agr., Bur. Plant Ind., Bull.* 100, p. 57.

<sup>13</sup> Johnson: *Exp. Sta. Record*, 1896-'97, viii, p. 232.

<sup>14</sup> Bouilhac: *Ibid.*, 1899-'00, xi, p. 1916.

<sup>15</sup> Gosio: *Lafar's Technical Mycology*; Trans. by Salter, 1911, ii, p. 37.



arsenic. In fact one, *Penicillium brevicaulis*, was so adapted to grow in it and evolve diethylarsine that he proposed this as a means of detecting arsenic. Furthermore, one could easily pick out the mixtures containing the greater quantity of arsenic in this work, from the large quantities of mould upon their surfaces.

The very great stimulating effect of the *zinc arsenite* in the nitrification series was probably due as much to the stimulating influence of the zinc as to that of the arsenic. Lathan<sup>16</sup> found that small quantities of zinc stimulated algae. The same results have been obtained by Silberberg<sup>17</sup> working with higher plants. Ehrenberg's<sup>18</sup> work is of special interest in this connection, as he found that zinc stimulated plant growth in soils; but when the soil was sterilized, the zinc became toxic. This would indicate that the stimulation which has been noted by many investigators is probably only an indirect influence; and when the soil organisms were killed by heat, the toxic influence on the plant became perceptible.

*Lead arsenate* stimulates very greatly the nitrification in soil. Part of this stimulation is most likely due to the arsenic while some is due to the lead. Stoklasa<sup>19</sup> has shown that lead, when present in small quantities, stimulates the growth of higher plants. It is possible that the amorphous lead arsenate improves the texture of the soil and in so doing increases nitrification in it. Little if any effect could be attributed to the purely catalytic influence of lead, as Russell and Smith<sup>20</sup> found this to be very small. Again there is the possibility that some of the compounds inhibit the activity of injurious species. But these possibilities, and the question as to how much the results would vary in other soils, are problems which can be solved only by further work. Stoklasa<sup>21</sup> ascribed the observed stimulation of growing sugar beets, when arsenic and lead were applied to the soil, to the catalytic action of these elements on the chlorophyll apparatus of the plants. These results indicate that it was due to their influence on the biological transformation of the nitrogen in the soil.

<sup>16</sup> Lathan: *Bul. Torrey Bot. Club*, 1909, xxxvi, p. 285.

<sup>17</sup> Silberberg: *Ibid.*, 1909, xxxvi, p. 480.

<sup>18</sup> Ehrenberg: *Landw. Vers. Stat.*, 1910, lxxii, p. 15.

<sup>19</sup> Stoklasa: *Compt. rend.*, 1913, clvi, p. 153.

<sup>20</sup> Russell and Smith: *Jour. Agr. Sci.*, 1906, i, p. 444.

<sup>21</sup> Stoklasa: *Expt. Sta. Rec.*, 1912, xxvi, p. 225.

Both ammonification and nitrification were greatly stimulated by *arsenic trisulfide*. It is likely that the sulfur played some part in this result. Demolon<sup>22</sup> attributed much of the fertilizing action of sulfur to its action on bacteria. The results which Russell and Hutchinson<sup>23</sup> obtained with calcium sulfide are interesting in this connection. They found that after thirty days there were five times as many organisms in soil to which calcium sulfide had been added as in the untreated soil, and that the yield of ammonia and nitrates in this time was one third greater in the treated soil than in the untreated soil. These results show considerable similarity to the data reported here for arsenic trisulfide; and most of the results obtained in this study may be interpreted by their theory<sup>24</sup>—that the soil contains another group of organisms which are detrimental to bacteria. If this theory be accepted, we must conclude that the soil bacteria are much more resistant to arsenic than are these other organisms, and that the soil organisms are able to function in the presence of very much larger quantities of arsenic than is this other class of organisms. For, while the antiseptics used by Russell and Hutchinson in their experiments were subsequently removed, this was not the case with the arsenic in this work. As large a quantity of water-soluble arsenic was found in the soil at the end as at the beginning of an experiment. Some of the observed stimulation was doubtless due to copper, lead, zinc, and sulfur, or whatever other foreign material was present in the insecticides. The constant occurrence of a stimulation in all the series points conclusively, however, to the fact that arsenic in some concentrations stimulates bacterial action. It must evidently occur in soil in large quantities before it becomes very toxic to the soil organisms.

#### IV. SUMMARY

One hundred parts per million of *sodium arsenate* may be applied to a soil rich in calcium and iron without materially decreasing the ammonifying or nitrifying powers of that soil. Smaller quantities may stimulate these activities.

<sup>22</sup> Demolon: *Compt. rend.*, 1913, clvi, p. 725.

<sup>23</sup> Russell and Hutchinson: *Jour. Agr. Sci.*, 1913, v, p. 173.

<sup>24</sup> Russell and Hutchinson: *Ibid.*, 1909, iii, p. 111.

*Zinc arsenite*, *lead arsenate* and *arsenic trisulfide* stimulate the ammonifying activities of a soil, and their toxicity is not very marked until comparatively large quantities of arsenic are present. The two former reduce the ammonifying and nitrifying activities only one-half when 1,120 parts per million of arsenic are present, while arsenic trisulfide exerts a stimulating influence upon the ammonifying activities of the soil in the lower concentrations and does not become very toxic even in the highest concentrations.

*Paris green* exerts marked toxicity on the ammonifiers, even when present in small quantities. When present in large quantities it practically stops ammonification in soil.

All these compounds stimulated nitrification, the stimulation being least for *Paris green* and greatest for *lead arsenate*.

Arsenic trisulfide and *Paris green*, when present in large quantities, nearly stopped nitrification.

Arsenic stimulated ammonification and nitrification, when it was present in soils in small quantities, but in very large quantities it was toxic. It is improbable, however, that *lead arsenate*, *zinc arsenite*, or *arsenic trisulfide*, will ever be applied to agricultural soil in quantities sufficient to become injurious to soil bacteria. *Paris green* may, but the quantity added would have to be large.

The stimulating activity of the various compounds added to the soil, upon ammonifying organisms and especially upon the nitrifying forms, is partly due to the anion and partly to the cation. Much of their action may be due to their influence upon injurious species.

Water-soluble arsenic may exist as such in soils to the extent of 82 parts per million without entirely stopping ammonification and nitrification. Large quantities of ammonia and nitric nitrogen may be produced in a soil containing 50 parts per million of water-soluble arsenic, which is a greater quantity than any ever found in an agricultural soil.

Measured in terms of their influence upon ammonification and nitrification as it takes place in soil, the toxicity of *lead arsenate* is the least. Next come *zinc arsenite* and *arsenic trisulfide*. The greatest toxicity is exerted by *Paris green*. From the results reported in the literature on the subject, this seems to be the sequence of toxicity when tests are made on the higher plants.

There is nothing in these results to indicate that arsenic trisulfide, or zinc arsenite, is as safe as lead arsenate for use as an insecticide. Arsenic trisulfide may be safer when first added to the soil, as is shown by its being almost insoluble when first applied and having practically no toxic influence upon ammonification; but, as bacterial action takes place in the soil, the arsenic of the arsenic trisulfide is much more soluble than that of lead arsenate, and becomes toxic to the nitrifying organisms when it is present in large quantities.

# THE NATURE OF HUMUS AND ITS RELATION TO PLANT LIFE\*

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Considerable progress, recently, in connection with our knowledge of the chemical nature of "humus" makes it desirable briefly to review the results obtained.

Up to a few years ago the generally accepted idea was that humus consisted of but a few organic compounds. This was largely due to the work of a number of investigators, such as Berzelius,<sup>1</sup> Detmer,<sup>2</sup> Braconnot,<sup>3</sup> Malaguti,<sup>4</sup> Terreil,<sup>5</sup> and especially Mulder<sup>6</sup> and his school, who held that humus consists of a few simple organic substances which are chiefly acid in their nature (or at least can be converted into acids by treatment with alkalies), and which are closely related to each other. Thus, according to Mulder, ulmic acid, the first product in the decomposition of organic matter, is gradually converted into humic acid, geic acid, apocrenic and crenic acids, in the order named, all of which consist of but three elements: carbon, hydrogen, and oxygen.

This conception of Mulder's and of contemporary writers may have been due, in part, to the facts that protein matters were then assumed to have a uniform<sup>7</sup> composition; that the known carbohy-

\* Published by permission of the Secretary of Agriculture. Based largely upon the work conducted during the last six years by the writer while he was connected with the Michigan and Iowa Agricultural Experiment Stations. Reported to the Biological Division of the American Chemical Society (see p. 89).

<sup>1</sup> Berzelius: *Lehrbuch d. Chemie*, 3. Aufl., 8 (1839).

<sup>2</sup> Detmer: *Landw. Versuchsstationen*, 14 (1871).

<sup>3</sup> Braconnot: *Ann. chim. phys.*, 12, 191 (1819).

<sup>4</sup> Malaguti: *Ibid.* [3] 54, 407 (1858); *Ann.* (Liebig), 17, 52 (1836).

<sup>5</sup> Terreil: *Bul. de la soc. chim.* [2] 44, 2 (1885).

<sup>6</sup> Mulder: *Ann.* (Liebig), 36, 243 (1840); *Chemie der Ackerkrume*; *Jour. f. pract. Chem.*, 21, 343 (1840).

<sup>7</sup> Kossel: *Berichte d. d. chem. Ges.*, 34, 3245 (1901).



drates and their disintegration products were comparatively few (which was also true of the protein products); and last, but not least, that the methods of research in organic and biological chemistry were inadequate.

Recent investigations have thrown enough light upon the chemical nature of humus or humus organic matter in the soil to demonstrate that it is a very complex material, which, in addition to dark colored humin substances, contains a large number of organic compounds displaying acid, basic, neutral and amphoteric characters.

The development of the idea of the chemical nature of humus stands in a certain relation to the development of the chemistry of carbohydrates and proteins out of which humus is formed in the soil.

Of the carbohydrates, mankind for centuries knew only cane sugar, which was originally obtained exclusively from the sugar cane. The same sugar was later discovered in the sugar beet (Marggraf, 1747), sorghum, maple tree and other plants. In addition to this sugar there were discovered, also, lactose (Bartoletti, 1615), glucose (Lowitz, 1792), fructose (Dubrunfaut, 1847), and so forth. At present we know a considerable number of sugars in the form of bioses, trioses, tetroses, etc., up to nonoses, *i. e.*, sugars which contain in their molecules from two to nine carbon atoms, respectively, and which occur, in part as such, in nature; the pentoses and hexoses and the corresponding polysaccharides being the most important.

As was demonstrated by many researchers, such sugars and, generally speaking, carbohydrates,<sup>8</sup> when treated with acids or alkalis, yield brown or black humin substances, whose physical and chemical properties remind one of soil humus to such a degree, that

<sup>8</sup> Malaguti: *Ann.* (Liebig), 17, 52 (1836); Berzelius, *Lehrbuch d. Chemie*, 3. Aufl. 8 (1839); Conrad and Guthzeit, *Ber. d. d. chem. Ges.*, 18, 439 (1885); 19, 2850 (1886); Sestini, *Gaz. chim. ii.*, 10, 121, 355.

Grote and Tollens, *Ann.* (Liebig), 176, 181 (1875); 202, 226 (1880); Pélégot, *Ann. chim. phys.* [2], 73, 208; Mulder, *Ann.* (Liebig), 36, 243 (1840); *Chemie der Ackerkrume*; O. Schmiedeberg: *Arch. expt. Path. und Pharmakol.*, 39, 1 (1897); Hoppe-Seyler: *Zeit. f. physiol. Chem.*, 13, 66 (1889); Samuely: *Beitr. chem. Physiol. und Path.*, 2, 355 (1902).

the artificial and natural products were considered by some as closely related,<sup>9</sup> by others even as identical.

When, however, dilute acids are applied, the carbohydrates yield a number of well defined intermediary products. Thus, the polysaccharides furnish first monosaccharides, these latter yield organic acids, etc. For raffinose, *e. g.*, we have: Raffinose (melitriose)  $\rightarrow$  melibiose (+ *d*-fructose)  $\rightarrow$  *d*-glucose + galactose. The resulting monosaccharides can yield, *e. g.*, lactic acid, butyric acid, alcohol, citric acid, etc., depending upon the conditions of transformation.

So far as proteins are concerned, it was first thought that they have a uniform composition and constant properties. Modern researches revealed the fact that the various proteins have different chemical composition and structure. Their gradual decomposition leads (through the stages of proteoses and peptones) chiefly to diamino and monoamino acids. And it is the latter compounds particularly that play a role in the formation of humin substances.

A number of investigators<sup>10</sup> have found that proteins when treated with acids yield humus-like substances. A further study of this phenomenon showed that it is particularly the diamino acid lysin,<sup>11</sup> and the monoamino acids tryptophan<sup>12</sup> and tyrosin (and glucosamin) that participate in the production of the melanoidins.<sup>13</sup> Hence, it is evident that plants containing proteins rich in tyrosin, tryptophan, lysin and glucosamin radicals will, everything else being equal, yield more humus than plants poor in those compounds.

When pure proteins are subjected to the influence of enzymes or to the activity of microorganisms, they are first hydrolyzed, chiefly to diamino acids and monoamino acids. The resulting primary amino acids are, especially under the influence of microbes, subjected to secondary changes which lead to the formation of humin substances, fatty and hydroxy acids, phenols, basic substances,

<sup>9</sup> Sostegni: *Landw. Vers.-Stat.*, 32, 9 (1885); André: *Bull. soc. chim.* [3] 21, 497 (1899); Eggertz: *Chem. Centralbl.*, 343 (1889).

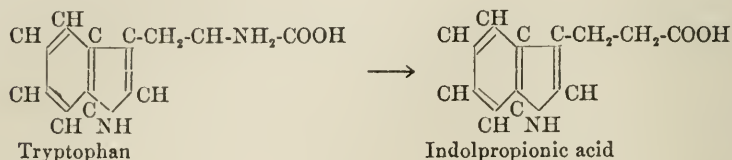
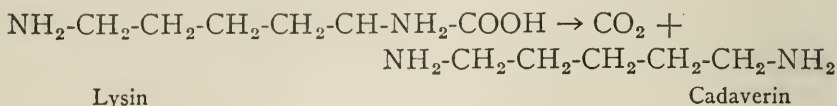
<sup>10</sup> Mulder: *Jour. f. pract. Chem.*, 21, 343 (1840); The Chemistry of Vegetable and Animal Physiology, trans. by Fromberg (Edinburgh and London), 1849, p. 153; Schmiedeberg: *Arch. f. exper. Pathol. u. Pharmacol.*, 39, 65 (1897); Panzer: *Zeit. f. physiol. Chem.*, 33, 131 (1901).

<sup>11</sup> Hart: *Zeit. f. physiol. Chem.*, 33, 355 (1901).

<sup>12</sup> Hopkins and Cole: *Journ. of Physiol.*, 27, 418 (1901); 29, 451 (1903).

<sup>13</sup> Samuely: *Hofmeister's Beiträge*, 2, 355 (1902).

etc. Thus, the splitting off of carbon dioxide from the diamino acids as well as of the  $\text{NH}_2$  group from the monoamino acids, leads to the formation of amines and acids respectively, as illustrated by the following equations:



In the case of nucleoproteins there result, in addition to protein products, purin derivatives and pyrimidin bases.

When carbohydrates are subjected to the influence of enzymes and bacteria, they also, as the result of primary hydrolysis, are first split into smaller carbohydrate molecules, which then may be further decomposed to alcohol, organic acids, etc.

In the same manner, fats, under the influence of similar agencies, are split into fatty acids and glycerol.

There is no reason to assume that the proteins, nucleoproteins, carbohydrates and fats in vegetable and animal remains, when subjected to the action of such agencies in soil, would not yield decomposition products similar to those that result in the case of pure proteins, nucleoproteins, carbohydrates and fats.

Recent investigations show that humus, using this word in its widest sense, is very complex, consisting of a large number of compounds. Contrary to the findings of earlier writers (see p. 17) humus contains, in addition to carbon, hydrogen and oxygen, also nitrogen, sulfur and phosphorus. It contains acids of well known composition and constitution, *e. g.*, monohydroxystearic,<sup>14</sup> dihydroxystearic, oxalic, succinic, acrylic, saccharic. It contains basic sub-

<sup>14</sup>Schreiner and Shorey: *Bul. Nos. 53 and 74, Bureau of Soils, U. S. Dept. Agr.; Jour. Amer. Chem. Soc.*, 32, 1674 (1910); *Proc. Eighth Intern. Congr. Appl. Chem.*, 15, 247 (1912).

stances, *e. g.*, diamino acids (Kossel's hexon bases),<sup>15</sup> purin<sup>16</sup> bases, and amins.<sup>17</sup> It contains a variety of "neutral" compounds, *e. g.*, hydrocarbons,<sup>18</sup> esters, aldehydes, as well as amphoteric substances like amino acids,<sup>19</sup> etc.<sup>20</sup> Moreover, there is very little doubt that the number of definite organic compounds which can be extracted from "soil organic matter" will be considerably increased within the next few years.

Mention may be made here of the fact that, of the compounds found in "soil organic matter," the amino acids and acid amides play a prominent role, for the reason that they are contained in predominant proportions in acid extracts of soils; and for the further reason that they represent an important source for the production in the soil of ammonia,<sup>21</sup> and hence of nitrates.

Considering that certain constituents (the ten well known elements) are absolutely indispensable for plant life, it is easy to understand why humus is called by many the "life of the soil." Not only does it contain most of the elements which are necessary for plant life, like nitrogen, phosphorus, sulfur, etc., but, what is of equally great importance, it affords a means for rendering more of the necessary inorganic elements available.

The carbon dioxide, nitric acid and sulfuric acid which result through oxidation of the elements carbon, nitrogen and sulfur in humus, are powerful agents for the extraction of indispensable elements (potassium, calcium, magnesium and others) from the rocks, thus converting rocks and rocky land into fertile arable soil.

<sup>15</sup> Jodidi: *Techn. Bul. No. 4* (1909), *Mich. Agr. Expt. Station; Research Bul. No. 1*, *Iowa Agr. Expt. Sta.* (1911); Jodidi and Wells: *Research Bul. No. 3*, *Iowa Agr. Expt. Sta.* (1911).

<sup>16</sup> Schreiner and Shorey: *Jour. Biol. Chem.*, **8**, 385 (1910).

<sup>17</sup> Shorey: *Proc. Eighth Intern. Congr. Appl. Chem.*, **15**, 249 (1912).

<sup>18</sup> Shorey: *Proc. Eighth Intern. Congr. Appl. Chem.*, **15**, 248 (1912).

<sup>19</sup> Jodidi: *Jour. Amer. Chem. Soc.*, **32**, 396 (1910); **33**, 1226 (1911); **34**, 94 (1912); Schreiner and Shorey: *Jour. Biol. Chem.*, **8**, 381 (1910); Robinson: *Techn. Bul. No. 7*, *Mich. Agr. Expt. Sta.* (1911); *Jour. Amer. Chem. Soc.*, **33**, 564 (1911).

<sup>20</sup> A good account of the compounds extracted from soils is contained in *Proc. Eighth Intern. Congr. Appl. Chem.*, **15**, 248-250 (1912).

<sup>21</sup> Jodidi, Kellogg and Snyder: *Research Bul. No. 9*, *Iowa Agr. Expt. Station* (1912); Jodidi: *Jour. of the Franklin Institute*, **175**, 245 (1913); *Ibid.*, **175**, 483 (1913); *Proc. Eighth Intern. Congr. Appl. Chem.*, **26**, 119 (1912).



It is well known that humus improves the physical condition of the soil. It increases, for instance, a soil's capacity to hold water, to retain valuable nitrogenous constituents, to resist corrosion. It binds the particles of sandy soils. It makes clayey soils friable, increasing at the same time their capacity to absorb the sun's rays and rendering the soil-temperature more uniform. In other words, humus makes the soil a more habitable and suitable home for the performance of the life functions of plants.

Thus, we find the humification process inserted into the chain of nature's cycles as a necessary link, without which the perpetual continuance of plant life cannot be conceived. Again, man's food, whether of vegetable or animal origin, is composed chiefly of proteins, fats, carbohydrates and mineral substances, all of which are contained in the plant and animal bodies. However, animal life is, in the last analysis, based upon the presence of plants, the digestion and assimilation of which give the material for the formation in the animal body of its organs and tissues. Again, the plants need for their life certain elements which are present in humus. Here we have, then, a cycle in which the physical life of man, as well as the existence of the animal and vegetable kingdoms, are brought into close connection with humus. So close is this relation that conditions indispensable for life are also necessary for decomposition of humus materials; extremes that exclude life also render decomposition impossible. There is practically no plant life in arctic regions or throughout the winter, and there is no decomposition under the same conditions. On the other hand, plant life is luxuriant in the tropics. There, too, decay is very rapid. The plant and the animal kingdoms need air for their life. The same air is indispensable for decomposition. Equally, neither plant life nor decomposition of organic substances is possible without water.

In the process of humification, nature has a powerful means for the utilization of vast amounts of waste materials for purposes of life. Or to put it in other words: It is the humification of vegetable and animal remains that makes them available for new generations of plants.



## CLEAVAGE OF BENZOYLALANINE AND ACETYL-GLYCINE BY MOLD ENZYMES\*

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The readiness with which certain aromatic acids, in which the carboxyl group is attached to a cyclic nucleus, conjugate with glycine in the animal body is well known. Among the substances which undergo this synthesis the most familiar is benzoic acid and its substitution products. The reaction is, however, not limited to homocyclic compounds, since both five and six membered heterocyclic derivatives, among which may be mentioned pyromucic, thiophenic and pyridinic acids, also unite with glycine.

A reversal of this reaction takes place under the influence of certain enzymes. Such enzymes occur in plants as well as in animal tissues. One of us, in collaboration with Neidig, has shown that enzyme preparations from some of the lower fungi can bring about the hydrolysis of hippuric acid<sup>1</sup> and also that of pyromucuric acid.<sup>2</sup>

It was thought possible, however, that the enzymic hydrolysis might be of wider application than the corresponding synthesis. In the animal organism the best known conjugations are those in which the substance to be excreted is united with glycine, glucuronic acid, sulfuric acid or cysteine. Homologues of glycine do not enter into synthetic reactions with the formation of excretory products, nor do acid radicals of the aliphatic series unite with glycine. Considering the diversity of aromatic radicals capable of combining in this way with glycine and not with the other amino acids, the question arises as to what determines the specificity of the reaction, and whether the corresponding hydrolysis would be equally specific. For instance, is the cleavage of such compounds dependent upon the

\* Read at the Rochester meeting of the American Chemical Society, Sep. 10, 1913. (Page 83.)

<sup>1</sup> Dox and Neidig: *Zeitschr. f. physiol. Chem.*, 1913, lxxxv, p. 68.

<sup>2</sup> Dox and Neidig: *BIOCHEM. BULL.*, 1913, ii, p. 407.

presence of the glycine group or the presence of an aromatic acid radical? Or does hippuric acid simply represent a type of substituted amino acids, all of which are hydrolyzed by the same enzyme?

With the view of throwing some light on this question, benzoylalanine and acetylglucine were subjected to the action of enzyme preparations capable of hydrolyzing hippuric acid. Benzoylalanine may be regarded simply as a homologue of hippuric acid. Neither this substance nor acetylglucine, as far as we are aware, occurs in nature nor does either result from any known biological process.

Mold cultures were made as previously described<sup>3</sup> and the press juice allowed to act upon the sodium salt of benzoylalanine and acetylglucine respectively. Since the experiments were conducted exactly as outlined in our previous paper, the details will not be repeated here. The formol titration was made after the enzyme and substrate had been in contact for two weeks at room temperature. The results are given in the accompanying tables.

TABLE I  
Data on the cleavage of benzoylalanine

Source of enzyme	Titration: $n/10$ Ba(OH) <sub>2</sub> , c.c.	Control: $n/10$ Ba(OH) <sub>2</sub> , c.c.	Difference, c.c.	Cleavage, %
<i>Aspergillus niger</i> . . . . .	7.41	4.45	2.96	22.8
<i>Aspergillus clavatus</i> . . . . .	13.17	10.00	3.17	24.4
<i>Aspergillus fumigatus</i> . . . . .	8.46	5.28	3.18	24.5
<i>Cladosporium herbarum</i> . . . . .	12.95	10.14	2.81	21.6
<i>Fusarium oxysporium</i> . . . . .	10.66	8.09	2.57	19.8
<i>Penicillium roqueforti</i> . . . . .	11.31	9.65	1.66	12.8
<i>Penicillium expansum</i> . . . . .	9.96	8.13	1.83	14.1

TABLE 2  
Data on the cleavage of acetylglucine

Source of enzyme	Titration: $n/10$ Ba(OH) <sub>2</sub> , c.c.	Control: $n/10$ Ba(OH) <sub>2</sub> , c.c.	Difference, c.c.	Cleavage, %
<i>Aspergillus niger</i> . . . . .	28.92	10.62	18.30	86.93
<i>Aspergillus clavatus</i> . . . . .	20.05	6.79	13.26	62.99
<i>Aspergillus fumigatus</i> . . . . .	10.79	2.78	8.01	38.09
<i>Cladosporium herbarum</i> . . . . .	1.38	1.76	.....	none
<i>Fusarium oxysporium</i> . . . . .	22.56	6.43	16.13	76.62
<i>Penicillium roqueforti</i> . . . . .	13.73	2.03	11.70	55.58
<i>Penicillium expansum</i> . . . . .	25.33	6.53	18.80	89.31

<sup>3</sup> Dox and Neidig: Loc. cit.

Both benzoylalanine and acetylglutamine are hydrolyzed by an enzyme present in lower fungi. In the case of benzoylalanine the cleavage is considerably less than in that of acetylglutamine. A possible explanation of this difference may be the fact that the racemic mixture was employed and the enzyme was specific for only one isomer. This, however, cannot be stated with any certainty since optical studies were not made. It appears probable from the above results that the enzymic cleavage of substituted amino acids is not limited to compounds strictly analogous to hippuric acid, which occur as excretory products. The reaction is therefore not specific for glutamine derivatives, nor for benzoyl or similar radicals containing a cyclic nucleus.

## A COLOR REACTION OF GLYCINE WHEN BOILED WITH CHLORAL HYDRATE

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Considering the color reaction of triketohydrinden hydrate when boiled with amino acids, I was led to investigate the possible color reactions of other substances supposed to have two  $\text{—OH}$  groups attached to one carbon atom, when boiled with solution of amino acid. Only glycine has been studied. This report is a preliminary one.

The materials used in the experiments were the purest procurable in the market.

An aqueous solution of glycine in a beaker was treated with chloral hydrate in substance and boiled for five minutes. The solution assumed a dark red color, which was very marked. Aqueous solutions of glycine and chloral hydrate boiled separately remained colorless.

Glycine in dilute aqueous solution (1 to 5,000), treated in this way, yielded a distinct dark red color. A weaker solution of glycine (1 to 10,000) yielded faint amethyst color.

Phenol, glycerol, resorcin, acetone, ethyl alcohol, glyoxylic acid, orthophosphoric acid, and chloral itself, when boiled with aqueous solution of glycine, yielded no color.

Acetone boiled with barium hydroxid sol. and then with glycine sol., yielded a green color which changed to dark red in thirty minutes. A cold saturated solution of glycine in water was treated with chloral hydrate in substance and boiled to half the original volume. A port-wine colored solution resulted which, when treated with ether and extracted, yielded its color in part to the ether. The ether solution was evaporated over an incandescent lamp; there resulted a dark oily liquid which gave off pungent fumes.

This oily liquid, when cooled rapidly on a glass slide with solidi-

fied carbon dioxide, showed microscopic needles and leaf crystals which rapidly liquefied. The oily liquid yielded a green solution with strong hydrochloric acid. This solution was evaporated over a water bath. Portions of the syrupy fluid remaining just before dryness were placed on a slide with a platinum loop and allowed to cool. There formed microscopic crystals of brown leaves and balls.

A control was run by boiling chloral hydrate and extracting with ether. The ether solution was evaporated over an incandescent lamp, when typical chloral hydrate leaves and clumps crystallized out.

The nature of the various products has not been determined. They are now under investigation.



## STUDIES ON WATER DRINKING

### 15. The output of fecal bacteria as influenced by the drinking of distilled water at meal time

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**Introduction.** The first study of bacterial growth under the influence of water-ingestion was made by Fowler and Hawk (1), and somewhat later a more extended study of the problem was made by Mattill and Hawk (2). In the latter investigation it was found that the ingestion of large amounts (1,000 c.c.) of water with meals caused the protein constituents of the food to be more fully utilized as shown by a decrease in all forms of nitrogen in the feces, including bacterial nitrogen. When 500 c.c. of water were taken with meals no significant changes in protein utilization were evident. However, the data admitted of the negative conclusion that no undesirable effects followed the water-ingestion.

In each of the experiments mentioned, softened water (2<sup>a</sup>) had been employed. The beneficial influence exerted by the drinking of softened water at meal time having been indicated by these experimenters, the question naturally arose whether the drinking of distilled water at meal time would have a similar influence.

It has been quite generally supposed that distilled water, on account of its lack of salts, would consequently have an untoward influence on the processes of digestion and absorption. So far as we know, no experiment to prove the truth or falsity of this belief has ever been performed.

Findlay (3) wrote as follows concerning the influence of distilled water upon the tissues. "If tissues or cells are placed in distilled water, passage of water into the cells occurs owing to the difference of osmotic pressure. The cells swell up and may finally burst and die. A similar poisonous action on cells is observed when

distilled water is drunk. In this case the surface layers of the epithelium of the stomach undergo considerable swelling; salts also pass out, and the cells may die and be cast off. This may lead to catarrh of the stomach. It is to this action of pure water that the harmful effects of melted snow or ice is due, since freezing purifies the water. For this reason also, one of the springs of Gastein has come to be known as the Poison Spring, although its water is purer than ordinary distilled water."

If Findlay's argument regarding the pernicious influence of distilled-water ingestion is true, a very decided exception was noted in one of the fasting experiments made at the University of Illinois. In this instance a dog was fasted 117 days (4) and received, by means of a stomach tube, a daily ration of 700 c.c. of distilled water. The animal was then fed and brought back to normal weight, and again fasted for 104 days. At the end of this extremely long period of inanition, the organs and tissues of the animal were carefully examined. No signs of a deranged gastric mucosa were in evidence. If the toxic influence of distilled water is as pronounced as Findlay would have us believe, certainly a period of 117 days is a sufficiently long interval in which to demonstrate such an influence. This would appear to be particularly true in the case of a fasting animal, whose resistance to such toxic influence may have been lowered somewhat.

Granting the validity of Findlay's claim, his contention cannot be advanced as evidence of the harmful influence of drinking distilled water *with meals*. Because of the electrolyte content of the average diet, the distilled water would cease to act as distilled water soon after its entrance into the stomach. If distilled water is to be considered as having a toxic influence upon the gastric mucosa, such toxic effect must of necessity be more pronounced when the distilled water is introduced into an empty stomach. It will be apparent from the discussion which follows that we were able to detect no harmful influence exerted by the distilled water in the experiments herewith described.

Koeppé (5) has voiced the opinion that the catarrh of the stomach which may follow the excessive ingestion of ice arises because of the lack of salts in the water from the melting ice. Nocht (6)

and Winkler (7), on the contrary, cite several cases in which prolonged, distilled-water ingestion was unaccompanied by any harmful influences. Harlow (8) considers that the ingestion of water from glaciers leads to irritation of the mucosa of the gastrointestinal tract. Spitta (9) has recently expressed the opinion that the question whether distilled-water ingestion is harmful must be considered an open one. Very recently Oehler (10) has published data from a short series of tests upon white mice from which he draws the conclusion that distilled-water ingestion by these animals causes hemoglobinuria. The introduction of distilled water *into the circulation* will, of course, be followed by a transient hemoglobinuria. It is a little difficult to see, however, how the introduction of the fluid *into the stomach* can bring about such a condition. We expect to investigate the question shortly.

Incomplete digestion and absorption of the protein part of the food causes an increased elimination of nitrogen in the feces, or may result in an increased growth of bacteria in the lower intestine. Hence any experiment to show the course of bacterial development may have a direct bearing on the problems of digestion and absorption. It may be argued in a general way, for example, that an increase of bacteria shows a decreased digestive or absorptive efficiency, and a decreased bacterial content of the feces indicates a more efficient functioning of the organs of digestion and absorption.

**Description of the experiments.** METHODS. Fresh samples of feces were used for all analyses. Duplicate analyses were made in all cases, approximately 2 gm. of fecal matter being used in each determination. Total nitrogen was determined by the Kjeldahl method. The method used for bacterial nitrogen was in general the modification of MacNeal's method described by Mattill and Hawk (11). It differed in some of the details from the directions given by these workers. Two grams of fresh feces were weighed by difference into a 50 c.c. centrifuge-tube, rubbed up with 0.2 percent hydrochloric acid sol., and the bacterial matter brought into suspension in the usual manner. When the first serial centrifugation was completed, about one-half the suspension was transferred to a 100 c.c. centrifuge-tube. The experiment was then continued, using the larger tubes throughout the remainder of the experiment. The

use of the larger tubes shortens the time of the sedimentation, at the same time making as good a separation as is procured by the use of the smaller tubes. Another point of difference was the manner of transferring the bacterial substance to the Kjeldahl flasks after the final sedimentation. It was found, after some experimentation, that the bacterial substance settled more completely to the bottom of the centrifuge tube when the bacteria were suspended in sulphuric ether instead of ethyl alcohol. In all these analyses the sediment from the alcohol was therefore centrifuged with ether, the sediment being transferred to the Kjeldahl flask and the nitrogen determined in the usual way.

The centrifuge used in this experiment was run by an electric motor, which developed a speed of 1,400 revolutions per minute. It will be noted here that this is a slower rate of speed than is generally used. More will be said of this in a later connection.

SUBJECTS, PLAN, DIET, ETC. Two students, normal in every respect, were given a uniform diet for several days or until nitrogen equilibrium was reached, as shown by analyses of foods and excreta. During this period (preliminary), 100 c.c. of distilled water were taken with each meal. Besides this, 200 c.c. of distilled water were ingested by subject **V** at 10 A. M., at 3 P. M., and at 8.30 P. M. Subject **C** ingested a total of 400 c.c. at these hours. After the subjects had reached nitrogen equilibrium, they were placed on the "moderate water" diet, which differed from the preliminary only by the addition of 500 c.c. of distilled water at each meal. This made for subject **V** a total water-ingestion of 900 c.c. during the preliminary period, and of 2,400 c.c. during the "moderate water" period. The values for subject **C** were 700 c.c. and 2,200 c.c. respectively. The duration of the "moderate water" period was ten days. The subjects were then returned for an interval of five days to the diet of the preliminary period, this period being called the intermediate period. The "copious water" period was then begun, and continued five days. The diet during this period differed from that of the preliminary and intermediate periods by the addition of 850 c.c. of distilled water at each of the three meals, making a total daily ingestion of 3,450 c.c. for subject **V**, and of 3,250 c.c. for subject **C**. The diet of the preliminary



and intermediate periods was then resumed for five days, this constituting the final period.

In all cases charcoal capsules were used to separate the feces of the different periods. Analyses were always made on fresh individual stools, unless the amount was too small, in which case it was placed in a refrigerator in an air-tight receptacle; and upon the following day was mixed with the succeeding stool and analysis made on the composite sample.

Subject **V** was 24 years of age and weighed 58 kg. Subject **C** was 29 years of age and weighed 60 kg. The hours for meals were as follows: breakfast 7-7.30; dinner 12-12.30 and supper 6-6.30. The temperature of the water ingested by subject **V** was 14° C. whereas that ingested by subject **C** was 22° C.

The diet was the same for each subject and consisted of the following constituents, which were fed at each of the three daily meals: Graham crackers, 100 gm.; peanut butter, 15 gm.; butter, 25 gm.; milk 400 c.c.

**Discussion of results.** MODERATE WATER-DRINKING. *Subject C.* The decrease of fecal nitrogen from 1.236 gm. in the preliminary period (see Table 1) to 0.943 gm. in the "moderate water" period, with the corresponding drop in bacterial nitrogen from 0.729 gm. to 0.544 gm., was unexpected, since previous experiments in this laboratory (2) showed moderate water-drinking to have very little effect on the fecal-nitrogen excretion. In fact, the alterations in this excretion were heretofore so small that it was impossible to draw any positive conclusions. In this case, however, we have clear evidence to show that the processes of digestion and absorption have been improved by the drinking of an additional 1,500 c.c. of distilled water at meal time. The beneficial effects were not confined to the water period, but were carried over into the intermediate period. Although there was but 0.047 gm. decrease in bacterial nitrogen from the "moderate water" period to the intermediate period, the percent of nitrogen occurring as bacterial nitrogen was decreased from 57.67 percent to 53.78 percent. This confirms the previous findings that the influence of the "high water" ingestion was not confined alone to the interval during which it was being ingested.



TABLE I  
Subject C  
Preliminary Period.

Number of stool	Weight of stool, grams	Dry matter, per cent.	Amount of dry matter, grams	Fecal nitrogen, grams	Bacterial nitrogen, grams	Bacterial dry substance (calculated),* grams	Dry bacteria in dry feces (calculated),* per cent.	Bacterial nitrogen in fecal nitrogen, per cent.
1	41.0	27.85	11.42	0.819	0.505	4.608	40.35	61.66
2	103.0	27.86	28.70	1.911	1.184	10.803	37.64	61.96
3	83.0	26.40	21.91	1.079	0.634	5.785	26.40	58.76
4	60.5	25.77	15.60	0.737	0.422	3.854	24.68	57.26
5	179.5	26.68	47.90	2.158	1.219	11.122	23.22	56.49
6	53.5	25.77	13.78	0.713	0.413	3.768	27.34	57.92
Total . . . . .	520.5	.....	139.31	7.417	4.377	39.936	.....	.....
Average . . . . .	86.75	26.76	23.22	1.236	0.729	6.656	28.67	59.01

"Moderate Water" Period.

1	103.5	23.85	24.70	1.339	0.769	7.016	28.40	57.43
2	65.5	25.11	16.45	0.830	0.528	4.817	29.28	63.61
3	130.0	24.60	32.00	1.872	1.004	9.160	28.63	53.63
4	44.5	22.95	10.21	0.617	0.397	3.622	35.48	64.34
5	70.5	23.86	16.82	0.907	0.545	4.973	29.57	60.09
6	56.0	22.37	12.53	0.750	0.442	4.033	32.19	58.93
7	83.5	26.16	21.84	1.223	0.620	5.657	25.90	50.70
8	50.0	26.61	13.30	0.664	0.378	3.449	25.93	56.93
9	97.0	27.35	26.53	1.227	0.755	6.889	25.97	61.53
Total . . . . .	700.5	.....	174.38	9.429	5.438	49.616	.....	.....
Average . . . . .	70.1	24.89	17.44	0.943	0.544	4.962	28.44	57.67

Intermediate Period.

1	43.5	23.42	10.19	0.535	0.299	2.728	26.77	55.89
2	43.5	26.68	11.60	0.612	0.311	2.838	24.47	50.82
3	60.5	30.37	18.37	0.779	0.421	3.841	20.91	54.04
4	73.5	29.75	21.87	0.933	0.523	4.772	21.82	56.06
5	136.0	27.69	37.66	1.760	0.930	8.485	22.53	52.84
Total . . . . .	357.0	.....	99.69	4.619	2.484	22.664	.....	.....
Average . . . . .	71.4	27.92	19.94	0.924	0.497	4.533	22.74	53.78

"Copious Water" Period.

1	57.5	23.77	13.67	0.800	0.413	3.768	25.56	51.63
2	43.5	29.67	12.91	0.644	0.344	3.139	24.31	53.42
3	56.5	25.60	14.46	0.784	0.423	3.859	26.69	53.95
4	86.5	28.25	24.44	1.153	0.666	6.077	24.86	57.76
5	93.5	28.72	26.85	1.240	0.687	6.268	23.34	55.40
Total . . . . .	337.5	.....	92.33	4.621	2.533	23.111	.....	.....
Average . . . . .	67.5	27.34	18.47	0.924	0.507	4.622	25.03	54.81

Final Period.

1	72.0	27.20	19.58	0.998	0.536	4.890	24.97	53.71
2	66.5	27.17	18.079	0.941	0.541	4.845	25.81	55.95
3	72.5	25.18	18.25	0.937	0.540	4.927	26.00	57.63
4	74.5	23.20	17.28	0.948	0.539	4.918	28.46	56.86
5	72.5	22.68	16.44	1.001	0.571	5.210	31.69	57.04
Total . . . . .	358.0	.....	89.62	4.833	2.717	24.790	.....	.....
Average . . . . .	71.6	25.03	17.92	0.967	0.543	4.958	27.66	56.22

\* Previous tests showed that dry bacteria contain 10.96 percent of nitrogen.

*Subject V.* The differences here are not so great as in the case of subject **C**, but it will be seen, by examining Table 2, that the values for the intermediate period are in all cases less than for the preliminary period.

**COPIOUS WATER-DRINKING.** It will be recalled that this experiment was a continuation of the former, the intermediate period serving as the final period for the "moderate water" experiment, and as the preliminary period for the experiment on copious water-drinking at meal time.

As was mentioned before, the "copious water" period differed from the intermediate and final periods in that 850 c.c. of distilled water were added to the water-ingestion of each of the daily meals. This made a total water-ingestion of 3,450 and 3,250 c.c. per day, for subject **C** and for subject **V**, respectively.

*Subject C.* It is interesting to note that the values for total nitrogen, bacterial nitrogen and percent of bacterial nitrogen in fecal nitrogen, were less in all cases in the "copious water" period than in the "moderate water" period; also, that the values for the above were less in the final period than they were in the preliminary period. This would seem to indicate clearly that the drinking of moderate quantities of water with meals, 2,400 c.c. daily, had a beneficial influence, while the beneficial influence of larger quantities, 3,250 c.c. daily, was still more pronounced.

The most significant point regarding the bacterial-nitrogen excretion of subject **C** is the fact that the value for the preliminary period was much higher than that for any one of the four periods which followed. In other words the daily ingestion of 1,500 c.c. of water during the period of moderate water-ingestion caused a very pronounced reduction in the growth of intestinal bacteria; and this lowered development continued throughout the remainder of the experiment. The daily output of dry bacterial substance for the preliminary period (6.65 gm.) when compared with similar values for the other periods of the experiment (4.96, 4.53, 4.62, and 4.95 gm.) demonstrates this point very nicely.

*Subject V.* Another interesting comparison may here be made between the two subjects. As with subject **C**, the values for daily excretion of total fecal nitrogen, bacterial nitrogen and percent of

TABLE 2  
Subject V  
Preliminary Period.

Number of stool	Weight of stool, grams	Dry matter, per cent.	Amount of dry matter, grams	Fecal nitrogen, grams	Bacterial nitrogen, grams	Bacterial dry substance (calculated),* grams	Dry bacteria in dry feces (calculated),* per cent.	Bacterial nitrogen in fecal nitrogen, per cent.
1	51.5	21.25	10.94	0.842	0.466	4.247	38.82	55.32
2	189.5	17.96	34.04	2.274	1.489	13.586	39.91	65.47
3	198.5	17.42	34.58	2.370	1.366	12.463	36.04	57.65
4	75.0	16.64	12.48	0.887	0.574	5.234	41.94	64.68
5	86.0	19.54	16.80	1.069	0.687	5.269	37.32	64.27
6	85.0	21.11	17.94	1.056	0.635	5.797	32.31	60.17
7	84.5	21.90	18.50	1.072	0.609	5.558	30.04	56.83
8	240.0	17.32	41.57	2.530	1.364	11.445	29.94	53.91
Total . . . . .	1,010.0	.....	186.85	12.098	7.190	65.599	.....	.....
Average . . . . .	126.3	18.50	23.35	1.512	0.899	8.200	35.11	59.43

"Moderate Water" Period.

1	92.5	12.98	12.01	0.868	0.395	3.608	30.04	45.57
2	102.5	16.23	16.63	1.137	0.721	6.579	39.56	63.42
3	101.5	20.42	20.72	1.202	0.738	6.737	32.51	61.43
4	153.5	17.61	27.03	1.710	1.111	10.137	37.50	64.97
5	235.0	12.50	29.37	2.341	1.349	12.308	41.91	57.62
6	115.5	15.14	17.49	1.288	0.754	6.876	39.31	58.51
7	93.5	20.02	18.72	1.080	0.822	7.503	40.08	76.14
8	111.0	18.15	20.14	1.342	0.856	7.813	38.79	63.81
9	92.5	21.13	19.54	1.152	0.679	6.194	31.70	58.93
10	105.0	19.39	20.34	1.305	0.789	7.210	35.45	60.47
Total . . . . .	1,202.5	.....	201.99	13.425	8.215	74.965	.....	.....
Average . . . . .	120.3	16.80	20.20	1.343	0.822	7.497	37.11	61.19

Intermediate Period.

1	48.5	20.98	10.17	0.625	0.358	3.270	32.15	57.37
2	56.5	24.17	13.65	0.803	0.463	4.224	30.95	57.75
3	244.5	19.26	47.09	2.698	1.639	14.954	31.76	60.74
4	154.5	17.60	27.19	1.601	1.014	9.252	34.02	63.33
5	115.5	19.25	22.23	1.515	0.900	8.209	36.93	59.39
Total . . . . .	619.5	.....	120.33	7.241	4.374	39.909	.....	.....
Average . . . . .	123.9	19.42	24.07	1.448	0.875	7.982	33.17	60.41

"Copious Water" Period.

1	56.0	19.02	10.65	0.616	0.383	3.496	32.83	62.22
2	75.5	22.39	16.90	1.084	0.588	5.366	31.75	54.25
3	44.5	15.84	7.05	0.625	0.360	3.288	46.64	57.66
4	120.0	22.29	26.75	1.500	0.856	7.812	29.20	57.08
5	171.5	22.51	38.60	2.024	1.189	10.848	28.10	58.75
Total . . . . .	467.5	.....	99.95	5.849	3.376	30.810	.....	.....
Average . . . . .	93.5	21.38	19.99	1.170	0.675	6.162	30.83	57.72

Final Period.

1	162.5	20.29	32.97	1.890	1.004	9.160	27.78	53.12
2	124.5	19.19	23.89	1.432	0.781	7.122	29.81	54.51
3	56.5	21.07	11.90	0.714	0.420	3.835	32.22	58.87
4	214.0	16.13	34.52	2.222	1.258	11.478	33.25	56.61
Total . . . . .	557.5	.....	103.28	6.258	3.463	31.595	.....	.....
Average . . . . .	111.5	18.53	20.66	1.252	0.693	6.319	30.59	55.34

\* See note, bottom of Table 1.

bacterial nitrogen in fecal nitrogen, were less in the period of copious water-ingestion than in the "moderate water" period. Also, the values for these forms of nitrogen were less in the final period than in the preliminary period. Thus, data obtained from two subjects, while differing in detail, show the same general features, moderate amounts of water producing desirable results, while larger amounts have an augmented effect for the better.

**General discussion.** BACTERIA-EXCRETION. As Ehrenpfordt (13) has shown, the different values for bacterial nitrogen are caused by a diversity in the centrifugation procedure. With a high rate of speed the lighter bacterial substances are thrown out of suspension, while a slower rate of speed will cause more of these particles to remain in suspension during the course of a given length of time. Thus, it would appear to be almost impossible to stop at just the moment when all the non-bacterial substances have been removed and all of the bacteria are still in suspension. Ehrenpfordt has further stated that entirely comparable and trustworthy results are obtained by any given worker, using the same technic throughout. The absolute values are not so important as are the relations between values of different parts of an experiment obtained by a single experimenter.

Harris (12) as the result of recent experiments wrote as follows regarding the centrifugation procedure for bacteria determination: "I am of the opinion that if workers in this country, at least, are to continue using the method, some endeavor ought to be made to unify or standardize the technic; otherwise interlaboratory results cannot be considered comparable."

*Subject V.* Thirty-two stools were examined and analyzed for fecal bacteria-nitrogen, the method described by Mattill and Hawk (11) being employed with modifications as stated above. The percent of dry bacteria in the dry feces was found to vary from 27.78 percent to 46.64 percent, with an average of 33.36 percent. The ratio of bacterial nitrogen to fecal nitrogen varied from 53.12 percent to 76.14 percent, the average being 58.82 percent. The average daily excretion of bacterial dry substance was 7.232 gm.

*Subject C.* Thirty stools were examined and produced the following results: 26.51 percent of dry bacteria were found in the

dry feces. The values varied from 20.91 percent to 40.35 percent. The average percentage of bacterial nitrogen was 56.25, the low value being 50.70 percent and the high value 64.34 percent. The amount of bacterial dry substance excreted daily was 5.146 gm. The above facts may be summarized as follows:

	Bacterial dry substance, grams	Dry bacteria dry feces, per cent.	Bacterial nitrogen in fecal nitrogen, per cent.
Subject V.....	7.232	33.36	58.82
Subject C.....	5.146	26.51	56.25
Average.....	6.189	29.94	57.54

Nutrition experimenters have obtained the following results for the amounts of dry bacteria excreted daily:

Strasburger (14) .....	8.0	grams
Sato (15) .....	8.54	grams
Berger and Tsuchiya (16) .....	3.023	grams
MacNeal, Latzer and Kerr (17) .....	5.34	grams
Mattill and Hawk (2, 11) .....	8.27	grams
Blatherwick and Hawk .....	6.189	grams

Values obtained for the percentage of dry bacteria in dry feces are as follows:

Strasburger (14) .....	24.3	percent
Schittenhelm and Tollens (18) .....	42.0	percent
Lissauer (19) .....	8.67	percent
Harris (12) .....	9.18	percent
Tobaya (20) .....	11.22	percent
Sato (15) .....	24.39	percent
Berger and Tsuchiya (16) .....	12.6	percent
MacNeal, Latzer and Kerr (17) .....	26.9	percent
Mattill and Hawk (2, 11) .....	27.95	percent
Blatherwick and Hawk .....	29.94	percent

It is interesting to note, here, that the values for bacterial dry matter and for percent of dry bacteria in dry feces obtained from subject C are almost identical with those reported by MacNeal, Latzer and Kerr. Their values were 5.34 gm. and 26.9 percent respectively, and ours 5.146 gm. and 26.51 percent.



Since these analyses were all made at the same time, using the same centrifuge and the same technique, and uniformly higher results were obtained in the case of subject V throughout, it would appear that no hard and fast value can be laid down for the daily excretion of fecal bacteria. The questions of individuality, diet, and speed of centrifugation are important factors in bringing about the final results.

THE RELATIONSHIP OF URINARY INDICAN TO FECAL BACTERIA. Urinary indican is considered to be an index of intestinal putrefaction. If it is a true index then the relationship of the urinary indican excretion to the output of fecal bacteria ought to be of interest. For this reason the indican content of the urines from the subjects of this investigation was determined (21). A modification of Ellinger's method was used. Table 3 summarizes the corresponding values for indican (mg.) and bacterial nitrogen (gm.).

TABLE 3  
*Relation between urinary indican and fecal-bacteria nitrogen*

Constituent determined	Experimental period				
	Preliminary	"Moderate water"	Inter-mediate	"Copious water"	Final
Subject C.					
Indican (mg.).....	25.3	21.3	21.2	15.5	24.6
Bacterial nitrogen (gm.).....	0.729	0.544	0.497	0.507	0.543
Subject V.					
Indican (mg.).....	72.2	79.2	77.4	64.9	92.7
Bacterial nitrogen (gm.).....	0.899	0.822	0.875	0.675	0.693

The data in Table 3 indicate that copious water-drinking produced a marked reduction in the processes of intestinal putrefaction, as measured by the urinary indican output. The excretion of bacterial nitrogen in the feces was practically at its minimum simultaneously with the low indican values. In the period following the "high water" ingestion, this uniformity of relationship is lost inasmuch as the indican values undergo a sharp rise, whereas the bacterial values are increased only slightly.

It is evident that any uniform relationship between urinary indican and fecal-bacteria excretions, over any period of time and under various dietary conditions, is probably accidental. Indican, of course, has its origin in the indole which is produced from protein in the intestine through the activity of the indole-forming bacteria. If all the bacteria present in the intestine were indole-formers, then some definite relationship could reasonably be expected between the urinary indican and the fecal-bacteria nitrogen, provided that indican is a reliable putrefaction-index. However, inasmuch as there are several species of intestinal bacteria which are not classed as indole-organisms, it is readily seen how variations in the growth and development of these types of bacteria will influence the fecal-bacteria nitrogen values, but will have no influence upon the output of urinary indican.

**Conclusions.** When 500 c.c. of distilled water were added to the usual water-ingestion at each meal (100 c.c.), a decrease was noted in the amount of bacterial nitrogen excreted daily in the feces. This held true for two subjects. One subject responded more freely to the influence of the water than did the other. When the water-ingestion (100 c.c.) was increased by 850 c.c. per meal, a more pronounced decrease in the daily excretion of bacterial nitrogen was observed. This was more emphasized in the one case than in the other, but was very obvious in both.

Since the amount of bacterial nitrogen occurring in the feces may, in a way, be considered an index of the utilization of the protein in the food, we are led to conclude that there was a more efficient utilization of the proteins and hence better digestion and absorption when water was taken with meals. In both cases the beneficial results were not confined to the periods of increased water-intake, but continued into the periods following.

Two subjects fed upon a uniform diet for a period of slightly more than one month were found to have an average content of 57.54 percent of bacterial nitrogen in the fecal nitrogen. The average amount of dry bacteria excreted per day was 6.189 gm. The proportion of dry bacteria in dry feces was found to be 29.94 percent.

A decreased output of urinary indican was observed to accom-

pany the copious water-ingestion. There was, however, no definite relationship between the values for urinary indican and fecal-bacteria nitrogen under all conditions. A definite relationship would probably be accidental.

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## A NOTE ON THE DETERMINATION OF AMMONIA IN URINE

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Since the proposal by Folin<sup>1</sup> of his air-current method for the distillation of ammonia, this procedure has been almost universally adopted for estimating ammonia in urine, and in other fluids or mixtures where unstable nitrogenous substances may be present. The accuracy of this method, as employed under ordinary conditions, has never heretofore been questioned. Steel,<sup>2</sup> however, in a detailed examination of the Folin method under certain conditions, has called attention to the fact that the alkali employed by Folin (sodium carbonate) is incapable of completely decomposing magnesium ammonium phosphate, and in case the urine contains appreciable quantities of this substance, results are low and very irregular.

As urines are not infrequently met with which contain magnesium ammonium phosphate crystals, Steel proposed the modified technique of using one gram of sodium hydroxide and fifteen grams of sodium chloride, in place of the carbonate recommended by Folin. Steel shows conclusively that this mixture of sodium chloride and hydroxide will liberate ammonia quantitatively from magnesium ammonium phosphate, and details a number of experiments to show that substances other than ammonium salts which might be expected to occur in urine are not decomposed by this treatment so as to yield any ammonia.

Steel also gives figures of numerous determinations made on urines which contained no preformed magnesium ammonium phosphate crystals, to show that results are identical under such conditions, whether sodium carbonate or sodium hydroxide and sodium chloride be used to liberate the ammonia.

<sup>1</sup> Folin: *Zeit. f. physiol. Chem.*, 37, p. 161 (1902).

<sup>2</sup> Steel: *Jour. of Biol. Chem.*, 8, p. 365 (1910).

During the past two years we have made it a practice to run two ammonia determinations on each sample of urine, in one of which sodium carbonate was employed to liberate the ammonia, while in the second one Steel's mixture of sodium hydroxide and sodium chloride was used. Several hundred determinations have been made in this way, including both dog and human urines, and the figures thus obtained do not corroborate those reported by Steel for similar determinations. In every sample of urine analyzed we have obtained slightly higher figures where the hydroxide-chloride mixture was used, than where carbonate was employed.

There would be little object in including here our large mass of figures obtained in this connection. We may summarize them by stating that normal and pathological urines were used, very few of which were not strongly acid in reaction, and none of which showed the presence of any magnesium ammonium phosphate crystals. Where Steel's hydroxide-chloride mixture was used results were always higher by 0.1 to 0.8 c.c. of  $n/10$  solutions, amounting usually to from one to seven percent of the total ammonia present, than where carbonate was used.

The difference in the absolute amount of ammonia obtained by the two processes is obviously small, but the constant results raise a distinct question as to the essential accuracy of the two procedures employed. Does Folin's original process fail to yield *all* the ammonia from ordinary urines, or does Steel's modification decompose some additional urinary constituent in amount sufficient to yield distinctly measurable quantities of ammonia? This question puzzled us for a long time, but we believe that we have found the correct answer to it in a simple fact which has apparently been overlooked by both Steel and Folin in their work in this connection.

If carbonate be added according to Folin's directions to a sample of urine, and the aeration process be carried out for a few minutes, and a few drops of the mixture be then examined under the microscope, *abundant masses of magnesium ammonium phosphate crystals will be found.* We have obtained this result with every sample of urine examined. It can be readily verified by shaking a sample of urine with a little sodium carbonate for about two minutes, and examining the mixture under the microscope. Whether air passes



through the mixture is immaterial. As aeration proceeds, however, the phosphate is gradually decomposed, even by the carbonate, so that at the end of an hour the phosphate crystals may no longer be readily found. But once having had these crystals formed in considerable quantity we must conclude that the ammonia precipitated in this form is not quantitatively liberated again, because, as Steel has shown, starting with larger amounts of magnesium ammonium phosphate, one can scarcely recover fifty percent of the ammonia where carbonate is used. The abundant formation of the triple phosphate in the early stage of Folin's original method accounts fully for the slightly higher figures we have obtained where hydroxide was the alkali employed. It also accounts for the long time frequently necessary to obtain a maximal yield of ammonia in the Folin process. Using the same air-current, we have observed that either carbonate or hydroxide would give theoretical results at the end of an hour, using pure ammonium chloride solution, whereas in the case of urine, sodium hydroxide would still give a maximal yield in one hour, while sodium carbonate required nearly two hours to give its maximal yield.

In the light of the above-mentioned facts it is obvious that if Steel's observation that magnesium ammonium phosphate is not quantitatively decomposed by carbonate be correct (and we have ourselves repeatedly verified this conclusion), it follows as a matter of course that Steel's modification must give higher figures with all urines, and this is exactly what we have found to be the case. The difference appears to be in favor of Steel's modification. We cannot account for Steel's results in this connection.

As a conclusion we wish to point out that the question of triple phosphate formation, and its incomplete decomposition by carbonate, is one which applies to all urines in varying degrees, and we are of the opinion that whatever procedure is used, one should be adopted which will ensure complete decomposition of the phosphate whether originally present in the urine or not. In discussing Steel's findings Folin<sup>3</sup> recommended that urines which contained crystalline magnesium ammonium phosphate should first be treated with sufficient acid to dissolve the crystals, after which seven to ten grams of potas-

<sup>3</sup> Folin: *Jour. Biol. Chem.*, 8, p. 497 (1910).

sium oxalate and one gram of carbonate are added to twenty-five c.c., and the aeration process carried out as usual. This procedure will prevent reformation of the triple phosphate. Folin preferred this procedure to that suggested by Steel because he believes that carbonate is a far safer alkali to employ than is hydroxide. If, however, as we have pointed out above, a method should be employed which will prevent interference by magnesium ammonium phosphate in all urines, the addition of the large quantity of oxalate (seven to ten grams) in every determination, is somewhat of a draw-back. We are inclined to regard Steel's modification as a safe procedure until someone shows that it actually decomposes other urinary constituents to yield ammonia. We feel that it is distinctly preferable to carbonate alone, as advised in the original Folin process.

We may add that in his latest "microchemical" processes for ammonia, Folin and his collaborators<sup>4</sup> have provided for the addition of oxalate in all instances. The small volumes dealt with keep down the quantity of oxalate necessary. The figures reported by Folin and Macallum by the colorimetric method for ammonia in urine do not seem to us very satisfactory. While in many instances the agreement between the figures obtained by the old process and by the new is very close, in several cases the colorimetric values exceed the others by from five to twelve percent of the total ammonia present. Folin and Macallum state that "a trace of something capable of giving a color with Nessler's solutions continues to come long after all the ammonia has been removed," but that "the effect of this substance in actual ammonia determinations is so small as to be hardly, if at all, perceptible." So long as this substance capable of giving a color with Nessler's solution remains an unknown factor and where results may be as much as twelve percent higher by the colorimetric procedure, we should hesitate to regard this latter process as of equal accuracy with the older.

<sup>4</sup> Folin and Macallum: *Jour. Biol. Chem.*, 11, p. 523 (1912). Folin and Denis: *Ibid.*, 11, p. 532 (1912).

## STUDIES OF AERATION METHODS FOR THE DETERMINATION OF AMMONIUM NITROGEN

### 3. The ammonium nitrogen in beef\*

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**1. Introduction.** A MODIFICATION OF THE ORIGINAL FOLIN METHOD. Several years ago, during the course of a series of experiments on the effects of magnesium sulfate on metabolism, Steel<sup>1</sup> obtained anomalous results with the Folin method for the determination of urinary ammonium. The senior author, who was directing the experiments, suggested that these anomalous results might be due to the formation of ammonio-magnesium phosphate and to incomplete ejection, by the Folin method, of the ammonium from this compound. With Steel,<sup>2</sup> he then ascertained that the Folin method was inadequate for the determination of the yield of ammonia from urine that contained crystalline ammonio-magnesium phosphate. They found that sodium carbonate, in the proportions employed for the Folin method, was unable to disengage more than about 40 percent of the ammonium nitrogen from moderate quantities of ammonio-magnesium phosphate, whereas 0.5-1 gram of caustic alkali (instead of carbonate) promptly ejected all of it from large amounts of such phosphate. "Even in the presence of 50 times its weight of sodium carbonate and with 10 hours of thorough aeration, crystalline ammonio-magnesium phosphate cannot be completely decomposed by the Folin method of ammonia determination" (p. 81). Steel and Gies wrote as follows at the conclusion of their paper: "We hope in the near future to report a simple modification

\* The previous papers in this series were those by (1) Steel and Gies: *Jour. Biol. Chem.*, 1908, v, p. 71, and (2) Steel: *Ibid.*, 1910, viii, p. 365.

<sup>1</sup> Steel: *Ibid.*, 1908, v, p. 85. (Dissertation submitted in partial fulfilment of the requirements for the degree of Ph.D. at Columbia University.)

<sup>2</sup> Steel and Gies: *Ibid.*, 1908, v, p. 71.

of the Folin method that will yield all the ammonia (nitrogen) from ammonio-magnesium phosphate in the urine without producing ammonia from non-ammoniacal radicals" (p. 83).

The modification Steel and Gies had in mind when this intention was expressed, was, as their preliminary results had suggested, the substitution of caustic alkali for sodium carbonate. For some time, thereafter, Steel continued the work along these lines, in this laboratory, and found<sup>3</sup> that 0.5-1 gram of sodium hydroxid plus about 15 grams of sodium chlorid may be substituted for the sodium carbonate and sodium chlorid in the Folin method, for the complete ejection of ammonium from crystalline ammonio-magnesium phosphate in urine, without producing ammonia from amino radicals.

This modified Folin method has been in regular use in this laboratory ever since, for the determination of urinary ammonia, because it appears to be quite as efficient as the original Folin process in all respects and is certainly much more accurate when an appreciable quantity of ammonio-magnesium phosphate is present.

FOLIN'S CRITICISM OF THE PROPOSED MODIFICATION. Shortly after the publication of this finding, Folin wrote, in part, as follows:<sup>4</sup> "The possible occurrence of minute amounts of ammonium magnesium phosphate hardly warrants the substitution of sodium hydrate and sodium chloride for sodium carbonate and sodium chloride in all ammonia determinations as recommended by Steel. There can scarcely be any doubt but (!) that the carbonate is the safer reagent, and therefore to be preferred, unless weightier reasons can be found against it than the possible (!) occurrence of traces of the triple phosphate."

In expressing these opinions, Folin appears to have ignored the data which showed that ammonia was not evolved, by the NaOH-NaCl process, from such urinary constituents as allantoin, creatin, creatinin, glyocol, guanin, hippuric acid, leucin, taurin, tyrosin, urea, uric acid. The only support that Folin published for his opinion against the use of sodium hydroxid appears to be the following (p. 497): "The use of sodium hydrate in connection with the air current method for determining ammonia in urine was advo-

<sup>3</sup> Steel: *Jour. Biol. Chem.*, 1910, viii, p. 365.

<sup>4</sup> Folin: *Jour. Biol. Chem.*, 1910, viii, p. 497.



cated by Moritz several years ago, but it appears to have failed to meet with much approval: *Arch. f. klin. Med.*, lxxxiii, p. 567, 1905." This quotation virtually begs the question. Results of experiments *showing* "that the carbonate is the safer reagent," instead of comment on the failure of Moritz's suggestion "to meet with much approval," would have been convincing. With all due respect for Folin's opinion, we must await a *demonstration* of the superiority of sodium carbonate over sodium hydroxid in the aeration process, before we can agree with Folin that the modified method is not decidedly better than the old.

APPLICATION OF THE MODIFIED METHOD TO BEEF. In October 1910, soon after Dr. Steel's departure from this laboratory to accept a professorship at the University of Missouri, we began a series of experiments to determine the efficiency of the NaOH-NaCl method when applied to the determination of the ammonium nitrogen in beef. It appeared probable that the protein in meat would yield, under such conditions, particularly large proportions of ammonia as a result of hydrolysis by the caustic alkali; and we desired to ascertain the degree of deficiency, if any, of the method from this standpoint.

Most of the data recorded in this paper were obtained by the junior author in 1910-'11, but verifications were occasionally conducted by the senior author during that year and the ensuing one. Publication of the results has been purposely delayed in order that the data might accompany the succeeding paper by Dr. Smith,<sup>5</sup> whose work was begun in September, 1911.

2. Comparative efficiency of the  $\text{Na}_2\text{CO}_3$ -NaCl and NaOH-NaCl aeration methods for the determination of ammonium nitrogen. I. FRESH BEEF. In our direct comparison of the efficiency of the two aeration methods when applied to meat, we considered it possible that (*A*) the protein of meat might yield considerable ammonia by hydrolysis, and (*B*) that some of this ammonia might combine in part with magnesium and phosphate in the meat to produce ammonio-magnesium phosphate;<sup>6</sup> (*C*) that the ammonium

<sup>5</sup> Smith: BIOCHEMICAL BULLETIN, 1913, iii, p. 54.

<sup>6</sup> Crystals of ammonio-magnesium phosphate form promptly in muscle fibers exposed to ammonia fumes or immersed in ammoniacal solutions.



in normal muscle plasma occurs, in part, in the form of ammonio-magnesium phosphate or may readily pass into that compound;<sup>7</sup> (*D*) that the protein of meat, by combining with the alkali, might reduce the power of the latter to eject the nitrogen from ammonio-magnesium phosphate in the aeration process; and (*E*) that sodium hydroxid and sodium carbonate would behave very differently in degrees of hydrolytic influence on the protein or other unstable constituents, as well as in degrees of decomposing action on any ammonio-magnesium phosphate present to begin with or produced by the treatment. The work was planned under the influence of these possibilities.

*General method.* Hashed fresh beef (15–25 gm.), after accurate weighing, was thoroughly triturated with sand and water in a mortar, and transferred to a tall cylinder of suitable width. The total amount of added water was 100 c.c. About 2–3 gm. of sodium hydroxid or 4 gm. of sodium carbonate were added, kerosene promptly poured in, and *strong aeration immediately begun and continued 8–12 hours*. The force of the current was practically the same for each sample. Each alkali was used without addition of sodium chlorid, so that maximal effects, good and bad, might be elicited. The essential data are summarized in Table I.

TABLE I

*Data showing the yields of ammonium nitrogen from hashed beef, in comparative aerations with sodium hydroxid and sodium carbonate*

Specimen of hashed beef *	Date, 1911	Aeration with NaOH					Aeration with Na <sub>2</sub> CO <sub>3</sub>					Balance in favor of the NaOH method		
		Meat taken		Ammonium N 100 gm. meat			Meat taken		Ammonium N 100 gm. meat					
		1	2	1	2	Av.	1	2	1	2	Av.			
		Grams		Milligrams			%	Grams		Milligrams			%	
A	Mar. 15	26.896	27.379	36.44	27.61	0.032	21.727	.....	16.75	.....	0.017	0.015		
A	Mar. 16	24.230	27.257	28.89	29.79	0.029	27.261	26.552	13.87	13.71	0.014	0.015		
A	Mar. 18	19.146	17.470	21.21	28.05	0.025	20.932	21.912	16.72	15.33	0.016	0.009		
B	Mar. 25	19.596	16.526	50.368	50.998	0.051	.....	15.878	.....	41.79	0.042	0.009		
C	May 3	25.797	27.204	28.437	35.612	0.032	27.220	24.694	26.847	21.03	0.024	0.008		
C	May 5	16.085	15.969	30.463	31.561	0.031	22.424	22.234	25.410	28.90	0.027	0.004		

<sup>7</sup> In the putrefaction of meat, crystals of ammonio-magnesium phosphate appear early and accumulate rapidly.

\* Each reserve supply of hashed beef was kept frozen during the experiment.

In repetitions of the tests, with sodium carbonate and sodium chlorid in accord with Folin's original directions, and with sodium hydroxid and sodium chlorid plus moderate quantities of alcohol to reduce frothing, the senior author has obtained somewhat lower values for each method. Our results in the latter connection will be published in a discussion of another phase of the work.

It is obvious, from the data in Table 1, that the sodium hydroxid treatment yields somewhat more ammonia than the treatment with sodium carbonate. Whether some or all of the surplus was due to ammonia that had been produced from other sources than ammonium radicals will be discussed in a future consideration of related data. It may be said, in anticipation, however, that such surpluses appear to be derived wholly from ammonium radicals, especially when a moderate quantity of sodium chlorid is present and the periods of aeration are not excessive—they were *intended* to be in these tests. The sodium hydroxid data are somewhat higher than those already reported, for "fresh" meats, as obtained by methods that do not yield the full proportion of ammonia from triple phosphate (see page 65).<sup>8</sup>

II. AMMONIO-MAGNESIUM PHOSPHATE. In Table 2 we give results, obtained *independently* by the junior author, which confirm the earlier observations by Steel and Gies.

III. "MODIFIED" BEEF. *A. Hashed beef kept at refrigeration temperatures.* "Fresh" beef was prepared and refrigerated by our own methods, as for use in nutrition experiments.<sup>9</sup> Five preparations from as many independent supplies of fresh beef were made successively on Oct. 29, Oct. 31, Nov. 1, Nov. 3, and Nov. 5, 1910. Table 3 gives the analytic data obtained by the junior author with the NaOH-NaCl method.

Occasional comparative determinations with both methods by the senior author not only checked, in a general way, the data in Table 3, but also indicated that the higher the yield of ammonia with the NaOH-NaCl method, the lower the comparative yield with

<sup>8</sup> By "fresh" meat we mean, in the description of our general method (p. 48), beef that was *purchased* as such. The periods and conditions of previous refrigeration were unknown to us.

<sup>9</sup> Gies: *Amer. Jour. Physiol.*, 1901, v, p. 235; *Biochemical Researches*, 1903, i, repr. 1; *Proc. Soc. Exp. Biol. Med.*, 1908, vi, p. 27.

TABLE 2

*Data pertaining to the comparative yields of ammonium nitrogen, by the NaOH-NaCl and Na<sub>2</sub>CO<sub>3</sub>-NaCl aeration methods, from crystalline ammonio-magnesium phosphate\**

Phosphate taken	Aeration with NaOH		Aeration with Na <sub>2</sub> CO <sub>3</sub>		
	Total nitrogen		Phosphate taken	Total nitrogen	
	Found	Per gram		Found	Per gram
Gram	Milligrams		Gram	Milligrams	
0.2695	22.39	83.09	0.2724	7.14	26.21
0.3676	29.94	81.45	0.1564	3.92	25.06
0.4383	36.93	86.54	0.3109	8.269	26.60
0.5053	42.63	84.38	0.3968	8.689	21.81
0.4718	40.82	86.51	0.3394	8.409	24.78
0.4447	39.14	88.02	.....	.....	.....
Average .....	84.99		Average .....	24.89	
Average loss, per gram of phosphate, by the Na <sub>2</sub> CO <sub>3</sub> method, .....					60.10†

the Na<sub>2</sub>CO<sub>3</sub>-NaCl process—the greater the proportion of ammonio-magnesium phosphate in the refrigerated meat, the smaller the proportion of ammonia ejected by the Na<sub>2</sub>CO<sub>3</sub>-NaCl method. The data for the latter method are accordingly omitted from the tables.

TABLE 3

*Data pertaining to the yield of ammonium nitrogen, by the NaOH-NaCl method, from five preparations of hashed fresh beef, at intervals during prolonged periods of storage at different refrigeration temperatures*

Preparation I. A. Oct. 29, 1910-Jan. 5, 1911 at 26° F.

Date	Meat taken, grams			Ammonium nitrogen, milligrams			
	1	2	Average	1	2	Average	Per cent.
10-29, '10...	33.730	27.820	30.775	3.54	3.26	3.40	0.011
11-5, '10...	25.393	28.377	26.885	4.96	3.54	4.25	0.016
11-15, '10...	25.635	25.258	25.447	3.97	4.39	4.18	0.016
12-1, '10...	19.125	19.025	19.075	4.25	3.83	4.04	0.021
1-5, '11...	18.119	23.942	21.031	6.66	6.94	6.80	0.032

B. Jan. 5-Feb. 13, 1911 in ordinary refrigerator‡

1-23, '11...	31.973	33.185	32.579	57.39	57.25	57.32	0.174
2-13, '11...	23.647	22.398	23.023	75.70	70.85	73.28	0.313

\* Data pertaining to total nitrogen in the phosphate, as determined by the Kjeldahl method (0.3883, 0.2439 and 0.3465 gm. of phosphate taken): total nitrogen *per gram* of phosphate—87.34, 89.64 and 88.10 (av. 88.36) mg.

† A loss of 70.7 per cent.

‡ The temperature in the ordinary house refrigerator varied between 47-58° F.

TABLE 3 (continued)

Preparation II. A. Oct. 31, 1910-Jan. 9, 1911 at 26° F.

Date	Meat taken, grams			Ammonium nitrogen, milligrams			
	1	2	Average	1	2	Average	Per cent.
11-1, '10...	20.665	32.607	26.636	4.26	9.08	6.67	0.024
11-11, '10...	20.059	20.042	20.051	4.25	3.83	4.04	0.020
11-16, '10...	23.580	29.109	26.345	10.36	4.86	7.61	0.028
12-2, '10...	21.447	26.283	23.863	4.67	6.52	5.59	0.023
1-9, '11...	20.276	23.522	21.899	6.43	6.16	6.29	0.029

B. Jan. 9-Feb. 14, 1911 in ordinary refrigerator §

1-23, '11...	33.195	32.280	32.738	58.02	53.12	55.57	0.170
2-14, '11...	27.245	32.908	30.078	65.24	128.85	97.05	0.315

Preparation III. A. Nov. 1, 1910-Jan. 12, 1911 at 26° F.

11-1, '10...	30.158	35.551	32.855	12.90	8.65	10.77	0.034
11-11, '10...	19.254	25.082	22.168	5.22	5.39	5.30	0.024
11-21, '10...	27.610	28.740	28.175	6.23	6.80	6.52	0.023
12-5, '10...	17.832	21.147	19.490	4.67	5.39	5.03	0.026
1-12, '11...	20.716	22.932	21.824	10.07	8.93	9.50	0.044

B. Jan. 12-Feb. 15, 1911 in ordinary refrigerator

1-27, '11...	35.051	28.932	31.982	50.29	77.44	63.87	0.200
2-15, '11...	24.491	27.583	26.037	87.36	85.82	86.59	0.333

Preparation IV. A. Nov. 3, 1910-Jan. 13, 1911 at 26° F.

11-3, '10...	27.485	36.518	32.002	4.39	5.52	4.96	0.016
11-14, '10...	19.523	24.396	21.960	2.98	9.77	6.38	0.028
11-22, '10...	20.725	22.260	21.493	5.53	3.97	4.75	0.022
12-6, '10...	22.824	27.757	25.296	4.39	4.82	4.61	0.018
1-13, '11...	28.519	41.341	34.930	10.48	12.86	11.67	0.034

B. Jan. 13-Feb. 20, 1911 in ordinary refrigerator

1-27, '11...	28.059	28.155	28.107	55.78	45.01	50.40	0.179
2-20, '11...	31.995	32.596	32.296	96.74	102.20	99.47	0.308

Preparation V. A. Nov. 5, 1910-Jan. 17, 1911 at 26° F.

11-5, '10...	28.163	25.348	26.756	3.82	5.52	4.67	0.018
11-14, '10...	18.544	36.604	27.574	1.84	5.38	3.62	0.012
11-28, '10...	20.423	19.965	20.194	3.12	2.98	3.05	0.015
12-8, '10...	23.780	21.211	22.496	5.38	3.97	4.67	0.021
1-17, '11...	31.804	24.966	28.385	8.81	6.57	7.69	0.027

B. Jan. 17-Feb. 25, 1911 in ordinary refrigerator.

1-24, '11...	21.247	19.134	20.191	23.63	17.89	20.76	0.102
2-25, '11...	22.062	25.177	23.620	82.75	112.42	97.58	0.411

§ The temperature in the ordinary house refrigerator varied between 47-58° F.

*B. Hashed beef with definite additions of ammonio-magnesium phosphate of known nitrogen content.* The meat preparations referred to in Table 3 acquired a content of *crystalline* ammonio-magnesium phosphate after their storage in an ordinary refrigerator. We attributed the increased yield of ammonia nitrogen, as the examinations progressed (Table 3), to the accumulation of ammonium in the form of triple phosphate and other compounds, as a result of bacterial activity.<sup>10</sup>

The capacity of the NaOH-NaCl method to eject all the ammonium nitrogen from crystalline ammonio-magnesium phosphate *in meat* was tested directly by adding weighed amounts of such phosphate, with known nitrogen content, to meat whose yield of ammonia had been determined, in other portions, before the triple phosphate was admixed. The analytic data are presented in Table 4.

TABLE 4

*Data pertaining to the yield of ammonium nitrogen, by the NaOH-NaCl method, from meat and triple phosphate mixtures of known independent yields of ammonium nitrogen by the same method*

Preparation *	Date	Meat taken	Phosphate taken	Total yield of ammonium nitrogen		
		<i>A</i>	<i>B</i>	<i>A + B</i>		
		Grams	Gram	Found, mg.	Calculated, mg.†	Loss, mg.
I.....	12-9, '10	26.886	0.2398	18.4	26.0	7.6
	1-5, '11	32.513	0.3763	39.3	42.4	3.1
II.....	1-9, '11	25.942	0.3081	31.3	33.6	2.3
III.....	1-12, '11	28.703	0.3514	35.1	42.3	7.2
	1-12, '11	24.428	0.4566	47.2	49.5	2.3
IV.....	1-13, '11	24.018	0.5781	48.9	57.2	8.3
V.....	12-12, '10	25.957	0.2954	28.2	30.4	2.2
	12-12, '10	24.489	0.2734	21.8	28.2	6.4
	1-17, '11	28.243	0.3604	35.3	38.2	2.9
	1-17, '11	29.584	0.3393	31.7	36.5	4.8

<sup>10</sup> The meat was ordinary hashed beef, which had been thoroughly mixed by hand before refrigeration. No attempt was made to prevent introduction of bacteria.

\* The preparations referred to in Table 3 were used.

† The calculated total was derived, for the meat, from the data for the *nearest date* (Table 3); for the phosphate, from the aeration data in Table 2. Thus, for the first total (26.0 mg.) we calculated: (a)  $26.886 \times 0.21 = 5.646$ ; (b)  $0.2398 \times 85 = 20.383$ ; (c)  $5.646 + 20.383 = 26.029$ . It is obvious that such calculations are at best close approximations and that the average "loss" may be due, in part, to overcalculation.



The data in Table 4 suggest that the protein of the meat interfered with *complete* liberation of the ammonium nitrogen from the very large proportions of triple phosphate present in each case, but the probability of overcalculation of the amounts of ammonium nitrogen in the mixtures is against that indication. (See footnote, Table 4.) The data in Table 4 also suggest that ammonia was not produced from the protein of the meat.

**3. General conclusions.** Ignoring, for the present, certain considerations which the senior author intends to discuss in a subsequent issue of the *BIOCHEMICAL BULLETIN*, we conclude that the NaOH-NaCl method for the determination of ammonium nitrogen in meat is more accurate than the  $\text{Na}_2\text{CO}_3$ -NaCl process. This greater degree of accuracy we attribute to the capacity of the NaOH-NaCl method to eject, as ammonia, all the nitrogen in ammonio-magnesium phosphate, whether crystallized or dissolved. It is evident, also, that the NaOH-NaCl method is particularly suitable for the study of meat subjected continuously to prolonged periods of cold storage, because of the completeness with which the nitrogen of ammonio-magnesium phosphate may be removed and obtained as ammonia, and because any deficiencies of the method, especially as compared with the  $\text{Na}_2\text{CO}_3$ -NaCl process, induce plus errors—errors of the kind that would tend to suggest putrefactive changes very early, if any such changes were in progress.

The ammonia determinations in the work on fish described by Smith<sup>11</sup> and by Perlzweig and Gies,<sup>12</sup> in the two succeeding papers, were based on these findings. Their results with the NaOH-NaCl method give special emphasis to the foregoing conclusions.

[The preceding paper by Benedict,<sup>13</sup> which was received on the day the manuscript of this number of the *BULLETIN* was forwarded to the printer, also has an important bearing on these deductions. *Ed.*]

<sup>11</sup> Smith: *BIOCHEMICAL BULLETIN*, 1913, iii, p. 54.

<sup>12</sup> Perlzweig and Gies: *Ibid.*, p. 69.

<sup>13</sup> Benedict and Osterberg: *Ibid.*, p. 41.

# A STUDY OF THE INFLUENCE OF COLD-STORAGE TEMPERATURES UPON THE CHEMICAL COMPOSITION AND NUTRITIVE VALUE OF FISH

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## I. INTRODUCTION

With the invention of the ammonia machine for the production of low temperatures, the cold-storage industry may properly date its beginning. Although the use of low temperatures for the preservation of foodstuffs has long been recognized, it is only recently that careful studies have been made of the effects upon food products of long periods of cold storage.

Among the first to note the effect of cold upon foods was Tellier,<sup>1</sup> who observed that meat stored at from  $-2^{\circ}$  to  $+3^{\circ}$  C. retained its freshness. Bouley<sup>2</sup> also found that at a temperature of  $-2^{\circ}$  to  $+3^{\circ}$  C., meat kept for an indefinite period so far as putrescence was concerned, but not from the standpoint of edibility. Grassman<sup>3</sup> found that meats kept for eight months at a temperature of  $-2^{\circ}$  C. to  $-4^{\circ}$  C. did not deteriorate. He claimed that refrigerated meats may be cooked in less time than the fresh materials.

A comparative study of the chemical composition of fresh and cold-stored foods was made by Girard,<sup>4</sup> who studied the phosphorus content of vegetables and some animal products, such as pork, mutton, beef, eggs and milk. Gautier<sup>5</sup> made a very detailed study of the difference between fresh and cold-stored beef and

<sup>1</sup> Tellier: *Rev. d. Hyg.*, 1897, xix, p. 298.

<sup>2</sup> Bouley: *Compt. rend.*, 1874, lxxix, p. 739.

<sup>3</sup> Grassman: *Landw. Jahrb.*, 1892, xxi, p. 467.

<sup>4</sup> Girard: *Compt. rend.*, 1896, cxxii, p. 1387.

<sup>5</sup> Gautier: *Rev. d. Hyg.*, 1897, xix, p. 289.

mutton. He found 1 per cent. less moisture in the cold-stored products than in the fresh, but no difference in digestibility.

The effect of cold-storage upon bacteria and enzymes in meat was studied by both Mai<sup>6</sup> and Müller,<sup>7</sup> who showed that putrefaction was prevented but that the action of the enzymes was not inhibited. In the more recent investigations of the effects of cold-storage, emphasis has been placed upon its influence on meat, poultry and game, and to some extent upon vegetables. Little, however, has been said concerning cold-stored fish. The gap in our knowledge at this point led to this investigation.

In 1861, Enoch Piper<sup>8</sup> established a plant in Beekman Street, New York City, for the freezing of fish by means of ice and salt. Davis,<sup>9</sup> in 1868, invented special pans for the freezing of fish, but used the same refrigerating agent. The first carload of frozen fish was shipped from Oregon to New York in 1883, but the quantity was very small compared with the large shipments today. As early as 1888, Russia had an important frozen-fish industry. Sturgeons and dolphins were the principal fish used and the freezing was generally conducted in cellars at the sea-shore.

The frozen-fish industry began in America in the early 90's. The first plant was established at Sandusky,<sup>10</sup> Ohio, in 1892. The industry progressed slowly at first because of a strong prejudice against cold-stored products and particularly against frozen fish. Salmon was at first practically the only fish frozen, but at the present time many varieties are refrigerated.

Each refrigerating concern may have its own particular method of freezing fish but the general practice seems to be to freeze the fish, dip them in water, and refreeze in order that they may be completely encased in ice. They are then stored at a temperature of  $-16^{\circ}$  C. The coating of ice prevents loss of water due to surface evaporation. This coating is renewed as occasion requires.

Much has appeared in the literature concerning processes for the production of low temperatures and methods for handling cold-

<sup>6</sup> Mai: *Zeit. Nahr. u. Genus.*, 1901, iv, p. 18.

<sup>7</sup> Müller: *Arch. f. Hyg.*, 1903, xlvii, p. 127.

<sup>8</sup> See Loverdo: *Le Froid Artificiel*, 1903, p. 401.

<sup>9</sup> Davis: *Ice and Refrigeration*, 1901, xxi, p. 93.

<sup>10</sup> *Ibid.*

stored products. Little, however, has been written concerning the effect of cold-storage upon the chemical composition of the flesh of fish.

The Report of the U. S. Commission of Fish and Fisheries, for 1888, contains data of analyses of American food fishes. The specimens were, for the most part, fresh fish, a few being preserved but none were cold-stored. More recent analyses of fresh fish have been made by Williams and by Ulrich.<sup>11</sup> Williams'<sup>12</sup> work was conducted from an economic standpoint, while that of Ulrich was a purely chemical study of the composition of fish flesh. It happens that both of these authors have analyzed specimens of fish belonging to species similar to those analyzed by us. Mention will be made of their results when our own are discussed.

The work here reported was undertaken with the hope of ascertaining what change, if any, fish muscle undergoes during long periods of cold-storage. In order that our experiments might be properly controlled, a preliminary study was made of the muscle of fresh fish.

## II. EXPERIMENTAL

**Preliminary handling of the fish.** The fish used were the fluke, also known as summer flounder (*Paralithys dentatus* Linn.), and the winter flounder (*Pseudopleuronectes americanus* Walb.), both of which were furnished by a reliable dealer. These fish were selected because their habits imply that they might be particularly prone to bacterial decomposition in cold-storage. The flounder is peculiarly a "bottom fish," in fact is in the mud or sand most of the time. The various lots of fish were taken from the dealer's ordinary commercial products, which had been handled from the water to Fulton Market (N. Y.), and in the cold-storage plant, in accordance with the practical methods of the trade. As soon as a catch arrived at the wharf, three fish were sent to the laboratory and twenty-four others put into a cold-storage plant. At the plant the fish were suitably dipped, frozen and cold-stored as usual. Those which came to the laboratory arrived packed with cracked ice in an

<sup>11</sup> Ulrich: *Arch. Pharm.*, 1911, ccxlix, p. 68.

<sup>12</sup> Williams: *Chem. News*, 1911, civ, p. 273.

ordinary willow basket. The basket was lined with a water-proof paper, covered with burlap and the whole wrapped in heavy manila paper. The time in transit from the wharf to the laboratory was a little over an hour. Very little of the ice melted en route and, with one exception, the fish were never in contact with free water in the basket.

Upon requisition, fish were taken from storage, wrapped separately in paper, and sent at once to the laboratory, where they arrived in a short time. No appreciable thawing took place in transit. The storage samples, if received during the winter months, were kept over night under paper covers in shallow pans at room temperature. For the summer months this method of thawing was modified by placing the fish in an ordinary refrigerator over night and then allowing them to remain for an hour at room temperature the next morning. In either case, as soon as the fish were completely thawed, the analyses were begun.

Each lot of fish furnished by the dealer was given a number by him. The tag also bore the date and, in the case of stored fish, both the date of receipt at, and the date of delivery from, the cold-storage plant.

In every instance before the fish was prepared for analysis, the general external appearance was observed and, upon dissection, the color and texture of the muscle were also noted. Fresh fish which have been out of the water for some time often show "clots" of slime over their bodies, and in their mouths and gills. Under such conditions the gills may be pale and the fins slightly reddened. When a frozen fish is allowed to thaw at room temperature its skin becomes distinctly dry after the water has evaporated, no slime ever forming. Its gills may be pale but the fins are not red. A slight yellowish brown discoloration, just under the skin, was noted in the case of stored fish; in fresh fish there were certain gray subcutaneous areas. A difference in the consistency of the muscle of the stored fish was also noticed, that of the fresh fish being the firmer. These observations apply only to fresh fish kept on ice from 48-72 hours and to cold-stored fish immediately after thawing.

**Analytic determinations and methods.** The analytic determinations may be conveniently considered under four headings: *First*—



water, total solids, organic matter, inorganic matter; *second*—ammonium nitrogen, total nitrogen, “soluble nitrogen,” “insoluble nitrogen,” “coagulable nitrogen,” “non-coagulable nitrogen;” *third*—lipins (per cent and acidity); *fourth*—reducing substances and acidity of aqueous extract.

1. The determination of *water* was made in the following manner: An accurately weighed sample, approximately 5 gm., was dried in a large porcelain crucible on a water bath for from three to four hours, after which it was placed in an air bath, at 110° C., and dried to constant weight.

In the determination of *ash*, the following precaution was taken to prevent volatilization of chlorides. After the organic matter had been completely charred over a low flame, an aqueous extract was made of the residue. This liquid was brought to the boiling point and allowed to cool somewhat, when it was decanted as carefully as possible through an ashless filter, most of the residue remaining in the crucible. After drying, the residue and filter were ignited over a bunsen burner to a white ash. The extract was then added to the residue in the crucible and evaporated to dryness on a water bath. Finally the crucible was heated over a low flame to remove residual carbonaceous matter. By this method the soluble salts were not subjected to the high heat of ignition.

Both *total solids* and *organic matter* were calculated from data obtained by the foregoing methods.

2. *Ammonium nitrogen* was determined by the following modification of Folin's method.<sup>13</sup> Fifty grams of fish muscle were ground in a mortar with sand. The finely ground meat was suspended in a mixture of equal volumes of 95 per cent alcohol and water in an aeration cylinder. The mixture of alcohol and water was used in order to prevent excessive frothing during aeration. The volume in each case was approximately 200 c.c. Fifty gm. of pure sodium chloride and 4 gm. of pure sodium hydroxide were added to each 200 c.c. of suspension. As soon as the alkali was added, very vigorous aeration was begun and continued for at least four hours.

*Total nitrogen* was determined by the Kjeldahl process. Oxidation was facilitated by the addition of a small piece of crystallin copper sulfate to the sulfuric acid.

<sup>13</sup> Steel and Gies: *Journal of Biological Chemistry*, 1908, v, p. 71; Steel: *Ibid.*, 1910, viii, p. 365; Shulansky and Gies: *BIOCHEMICAL BULLETIN*, 1913, iii, p. 45.

"Soluble nitrogen" was determined by the Kjeldahl method, in 10 c.c. of an aqueous extract prepared in the following manner: Twenty gm. of water were added to each gm. of fish taken, but in preparing the extracts, an allowance was made for the water content of the flesh, which was found to average 78.48 per cent. Approximately 50 gm. of flesh were used. After the extract-mixtures were prepared, they were shaken thirty times and allowed to stand over night. Then they were again shaken, allowed to settle and filtered. During filtration care was taken to prevent losses by evaporation.

"Non-coagulable nitrogen" was determined directly as follows: 100 c.c. of extract, prepared by the foregoing method, were heated gently to boiling and then treated with 2 c.c. of a 2 per cent solution of acetic acid. When the liquid had again been carried to the boiling point, the solution was filtered directly into a Kjeldahl flask. Into the beaker in which the precipitation had been made, were poured 50 c.c. of distilled water. This was brought to the boiling temperature and then used at once to wash the precipitate on the filter. The precipitate was washed twice in this manner, after which the total ("non-coagulable") nitrogen in the combined filtrate and washings was determined as usual.

From data obtained by the foregoing methods, the "insoluble nitrogen" and "coagulable nitrogen" were determined by difference.

3. To prepare flesh for the determination of its content of *lipins*, muscle was quickly removed from the fish, passed through a hashing machine, and the hash dried at room temperature before an electric fan, after which the residue was pulverized in a drug mill. Mixtures of aliquot portions of each powder were used in the extractions, which were made by the Soxhlet method upon 60 gm. charges, whenever practicable.

The *acidity* of the lipin mixture was determined by shaking the sample with 50 c.c. of 95 per cent alcohol to which 1 c.c. of 1 per cent phenolphthalein solution in 95 per cent alcohol had been added and titrating with  $n/5$  alkali solution. A blank was always run simultaneously on the alcohol.

4. The *reducing power of aqueous extracts* of fish muscle, after removal of the protein, was determined by Benedict's<sup>14</sup> method. The extract was made by treating each gram of fish with 4 gm. of water. Coagulable protein was removed by the method described above.

We always ascertained the degree of *acidity of the aqueous extracts*, as prepared for the various nitrogen determinations. Fifth normal

<sup>14</sup> Benedict: *Journ. Am. Med. Assn.*, 1911, lvii, p. 1193.

sodium hydroxide solution was titrated against 100 c.c. of the extract, using phenolphthalein as the indicator.

**Conduct of the examinations.** Our examinations of the fish were conveniently divided into three series: (I) On *fresh* fish, (II) on fish

TABLE I

*Series I. Fresh flounders. Percentage data, except as noted*

Fish No.	Water	Total solids	Organic matter	Ash	Ammonium N	Fish No.	Nitrogen					Reaction of aqueous extract*
							Soluble	Insoluble	Coagulable	Non-coagulable	Total	
A1	78.35	21.65	20.36	1.29	0.014	.....	.....	.....	.....	.....	3.26	
A2	78.80	21.20	19.97	1.23	0.014	.....	.....	.....	.....	.....	3.21	
A3	79.01	20.99	19.77	1.22	0.012	.....	.....	.....	.....	.....	.....	
B4	78.74	21.26	19.97	1.29	0.025	.....	.....	.....	.....	.....	3.27	
B5	78.62	22.38	21.09	1.29	0.022	.....	.....	.....	.....	.....	3.51	
B6	79.10	20.90	19.62	1.28	.....	.....	.....	.....	.....	.....	3.32	
C7	76.81	23.19	21.96	1.23	0.011	.....	.....	.....	.....	.....	3.58	
C8	79.52	20.48	19.23	1.25	0.026	.....	.....	.....	.....	.....	3.21	
C9	79.76	20.24	19.04	1.20	0.023	.....	.....	.....	.....	.....	3.21	
D10	77.88	22.12	20.90	1.32	0.025	.....	.....	.....	.....	.....	3.49	
D11	75.78	24.22	22.66	1.56	0.029	.....	.....	.....	.....	.....	4.04	
D12	80.40	19.60	17.37	1.23	.....	.....	.....	.....	.....	.....	3.70	
L34	81.03	.....	.....	.....	.....	E13	1.079	2.361	0.705	0.374	3.44	1.75
L35	82.49	.....	.....	.....	.....	E14	1.084	2.716	0.711	0.373	3.80	1.85
L36	81.56	.....	.....	.....	.....	E15	0.924	2.336	0.552	0.372	3.26	1.68
M37	81.51	.....	.....	.....	.....	F16	1.011	2.409	0.612	0.399	3.42	1.45
M38	80.13	.....	.....	.....	.....	F17	0.959	2.511	0.501	0.458	3.47	1.20
M39	81.66	.....	.....	.....	.....	F18	0.958	2.282	0.562	0.396	3.24	1.05
N40	82.49	.....	.....	.....	.....	G19	1.118	1.752	0.772	0.346	2.87	1.35
N41	82.22	.....	.....	.....	.....	G20	1.065	1.695	0.724	0.341	2.76	1.30
N42	81.32	.....	.....	.....	.....	G21	0.746	1.774	0.429	0.317	2.52	2.25
O43	82.78	.....	.....	.....	.....	H22	0.799	1.921	0.485	0.314	2.72	1.30
O44	80.32	.....	.....	.....	.....	H23	1.012	2.018	0.629	0.383	3.03	1.35
O45	80.87	.....	.....	.....	.....	H24	1.173	1.727	0.737	0.436	2.90	1.00
P46	81.46	.....	.....	.....	.....	I25	0.852	1.838	0.426	0.426	2.69	1.00
P47	82.14	.....	.....	.....	.....	I26	0.852	1.958	0.453	0.399	2.81	1.20
P48	83.00	.....	.....	.....	.....	I27	0.759	2.121	0.351	0.408	2.88	1.10
R49	82.42	.....	.....	.....	.....	J28	0.852	1.998	0.447	0.405	2.85	1.35
R50	81.27	.....	.....	.....	.....	J29	0.746	2.244	0.363	0.383	2.99	1.10
R51	82.91	.....	.....	.....	.....	J30	0.932	2.238	0.554	0.378	3.17	1.15
.....	.....	.....	.....	.....	.....	K31	0.985	2.025	.....	.....	3.11	1.28
.....	.....	.....	.....	.....	.....	K32	1.518	1.562	1.137	0.381	3.08	1.63
.....	.....	.....	.....	.....	.....	K33	0.825	2.275	0.445	0.380	3.10	1.48
Average	80.15	21.52	20.16	1.28	0.0195	.....	0.964	2.084	0.579	0.383	3.18	1.37

**Lipins**—Fish L34–R51, in three groups; aliquot portions of the fish in each group were extracted together:

*Total amount of lipins in the fresh flesh* (per cent)—0.386, 0.360, 0.392; *average*, 0.379.

*Acidity* (mg. of KOH to neutralize 1 gm. of lipins)—131, 147, 132; *average*, 136.

\* Expressed as c.c. of  $n/5$  sodium hydroxid solution required to neutralize 100 c.c. of extract.

stored for six months, and (III) on fish stored for nine months. The analytic determinations upon each series of fish were of the same kind, but for convenience they may be considered in three different groups.

TABLE 2

*Series II. Flounders after six months of cold storage. Percentage data, except as noted*

Fish No.	Water	Total solids	Organic matter	Ash	Ammonium N	Fish No.	Nitrogen					Reaction of aqueous extract*
							Soluble	Insoluble	Coagulable	Non-coagulable	Total	
A70	78.00	22.00	20.70	1.30	0.006	.....	.....	.....	.....	.....	3.57	
A71	78.28	21.72	19.47	1.25	0.011	.....	.....	.....	.....	.....	3.31	
A73	78.02	21.98	20.73	1.25	0.009	.....	.....	.....	.....	.....	3.47	
B74	77.06	22.94	21.59	1.35	0.034	.....	.....	.....	.....	.....	3.53	
B75	77.82	22.18	20.82	1.36	0.022	.....	.....	.....	.....	.....	3.43	
B76	77.80	22.20	20.93	1.27	0.010	.....	.....	.....	.....	.....	3.34	
C77	79.57	20.43	19.17	1.26	0.011	.....	.....	.....	.....	.....	3.19	
C78	79.72	20.28	.....	.....	0.016	.....	.....	.....	.....	.....	3.21	
C79	78.62	21.38	20.12	1.26	0.008	.....	.....	.....	.....	.....	3.41	
D80	79.29	20.71	19.41	1.30	0.015	.....	.....	.....	.....	.....	3.23	
D81	80.85	19.15	17.92	1.23	0.008	.....	.....	.....	.....	.....	3.09	
D82	79.33	20.67	19.39	1.28	0.008	.....	.....	.....	.....	.....	3.38	
D83	.....	.....	.....	.....	0.022	.....	.....	.....	.....	.....	.....	
D84	.....	.....	.....	.....	0.017	.....	.....	.....	.....	.....	.....	
D85	.....	.....	.....	.....	0.015	.....	.....	.....	.....	.....	.....	
L108	80.39	.....	.....	.....	.....	E86	1.145	2.395	0.714	0.431	3.54	1.33
L109	81.62	.....	.....	.....	.....	E87	0.799	2.581	0.430	0.469	3.38	1.43
L110	81.02	.....	.....	.....	.....	E88	0.945	2.485	0.572	0.373	3.43	1.38
M111	81.81	.....	.....	.....	.....	F99	0.959	2.101	0.586	0.373	3.06	1.25
M112	82.02	.....	.....	.....	.....	F100	0.959	2.251	0.597	0.362	3.21	1.10
M113	81.64	.....	.....	.....	.....	F101	0.907	2.313	0.545	0.362	3.22	1.20
N114	82.55	.....	.....	.....	.....	G102	0.746	2.244	0.437	0.309	2.99	1.30
N115	80.30	.....	.....	.....	.....	G103	0.825	2.015	0.483	0.341	2.84	1.10
N116	81.04	.....	.....	.....	.....	G104	.....	.....	.....	.....	2.95	1.10
O117	82.58	.....	.....	.....	.....	H105	0.864	1.926	0.566	0.298	2.79	1.00
O118	79.78	.....	.....	.....	.....	H106	0.770	1.870	0.474	0.296	2.54	1.00
O119	82.41	.....	.....	.....	.....	H107	0.833	1.777	0.588	0.245	2.61	0.90
P120	82.40	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
P121	82.54	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
P122	82.49	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
R123	80.54	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
R124	80.53	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
Average	80.13	21.30	20.01	1.29	0.0142	.....	0.887	2.179	0.545	0.351	3.19	1.17

Lipins—Fish L108–R124, in three groups; aliquot portions of the fish in each group were extracted together:

Total amount of lipins in the undried flesh (per cent)—0.362, 0.458, 0.277; average, 0.366.

Acidity (mg. of KOH to neutralize 1 gm. of lipins)—150, 138, 120; average, 136.

\* Expressed as c.c. of  $n/5$  sodium hydroxid solution required to neutralize 100 c.c. of extract.

The *first group* of determinations included water, ash, ammonium nitrogen and total nitrogen. The determinations were made upon fish from four of the dealer's lots in each of the three series of observations.

The *second group* of determinations, comprising total, soluble and non-coagulable nitrogen, together with the reaction of the aqueous extract, was made upon fish from seven of the dealer's lots (Series I).

TABLE 3

*Series III. Flounders after nine months of cold storage. Percentage data, except as noted*

Fish No.	Water	Total solids	Organic matter	Ash	Ammonium N	Fish No.	Nitrogen					Reaction of aqueous extract*
							Soluble	Insoluble	Coagulable	Non-coagulable	Total	
A125	78.06	21.99	20.59	1.40	0.027	.....	.....	.....	.....	.....	3.39	
A126	77.97	22.03	20.76	1.27	0.026	.....	.....	.....	.....	.....	3.44	
A127	78.55	21.45	20.31	1.14	0.013	.....	.....	.....	.....	.....	3.29	
B128	79.48	20.52	19.34	1.18	0.022	.....	.....	.....	.....	.....	3.34	
B129	77.82	22.18	20.89	1.29	0.010	.....	.....	.....	.....	.....	3.55	
B130	79.14	20.86	19.67	1.19	0.019	.....	.....	.....	.....	.....	3.31	
C131	78.70	21.30	20.05	1.25	0.024	.....	.....	.....	.....	.....	3.28	
C132	77.65	22.35	21.12	1.23	0.032	.....	.....	.....	.....	.....	3.48	
C133	79.37	20.63	.....	.....	0.032	.....	.....	.....	.....	.....	3.54	
D134	76.74	23.26	21.73	1.53	0.017	.....	.....	.....	.....	.....	3.79	
D135	79.00	21.00	20.73	1.27	0.021	.....	.....	.....	.....	.....	3.35	
D136	78.97	21.03	19.72	1.31	0.012	.....	.....	.....	.....	.....	3.33	
L149	82.45	.....	.....	.....	.....	E137	1.074	2.046	0.741	0.333	3.12	1.87
L150	84.24	.....	.....	.....	.....	E138	1.127	2.483	0.719	0.408	3.61	1.85
L151	80.55	.....	.....	.....	.....	E139	1.043	2.507	0.592	0.451	3.55	1.63
M152	73.98	.....	.....	.....	.....	F140	0.820	2.260	0.466	0.354	3.08	0.95
M153	80.87	.....	.....	.....	.....	F141	0.913	.....	0.542	0.371	.....	1.35
M154	81.49	.....	.....	.....	.....	F142	0.966	2.364	0.603	0.363	3.33	1.10
N155	83.02	.....	.....	.....	.....	G143	.....	.....	.....	.....	2.99	0.90
N156	81.76	.....	.....	.....	.....	G144	0.859	2.121	0.548	0.311	2.98	0.90
N157	81.68	.....	.....	.....	.....	G145	0.895	2.095	0.519	0.376	2.99	0.97
O158	81.82	.....	.....	.....	.....	H146	0.966	1.264	0.655	0.311	2.23	0.97
O159	81.69	.....	.....	.....	.....	H147	0.806	2.064	0.511	0.295	2.87	0.88
O160	82.38	.....	.....	.....	.....	H148	0.859	2.071	0.548	0.311	2.93	1.20
P161	81.90	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
P162	82.18	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
P163	82.51	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Average	80.24	21.55	20.45	1.28	0.0213	.....	0.937	2.128	0.586	0.353	3.11	1.23

Lipins—Fish L149-P163, in four groups; aliquot portions of the fish in each group were extracted together:

Total amount of lipins in the undried flesh (per cent)—0.442, 0.497, 0.391, 0.442; average, 0.443.

Acidity (mg. of KOH to neutralize 1 gm. of lipins)—111, 130, 139, 130; average, 127.

\* Expressed as c.c. of *n*/5 sodium hydroxid solution required to neutralize 100 c.c. of extract.



When this group of determinations was repeated on Series II and III, four dealer's lots were used for each series.

The *third group* consisted of determinations of lipins, water and reducing power. Because of the small percentage of fat in the fish, all of the dealer's lots (six) in this group were drawn upon in each of the three series of observations.

In performing a particular set of analyses, samples of flesh were uniformly taken, as nearly as possible, from the same region. The selected parts were in the right angles made by a line running from the head to the tail and a line perpendicular to it about midway between the mouth and the tail. The skin on the back was opened, turned over, and flesh taken from all depths to the bone. Flesh near the viscera, as well as remote from them, were included. The skin was not analyzed.

For convenience in consulting the data, the following plan of tabulation was adopted. Each capital letter in the accompanying tables represents a dealer's lot of fish. The numeral following the capital letter indicates an individual fish. Thus, **B**<sub>5</sub> (Table 1) represents a particular fish that was *fresh* when analyzed. **B**<sub>75</sub> (Table 2) indicates a particular fish of the same lot which had been placed in cold storage and *analyzed six months later*. The capital letter also indicates, in terms of the appended summary, the date (in 1911) when a particular fresh fish was subjected to analysis (or placed in cold storage):

A-Sept. 9.	E-Oct. 18.	I-Nov. 27.	M-Dec. 6.
B-Sept. 29.	F-Nov. 1.	J-Nov. 29.	N-Dec. 8.
C-Oct. 3.	G-Nov. 22.	K-Dec. 1.	O-Dec. 11.
D-Oct. 10.	H-Nov. 24.	L-Dec. 4.	P-Dec. 13.
			R-Dec. 19.

### III. DISCUSSION OF RESULTS

**Water.** From the tables it will be seen that, beginning with lot **L**, there is an increase in content of water. The fish in lots **A** to **D** were flukes or summer flounders, while those in lots **L** to **R** were winter flounders. Apparently the water-content of the winter flounder is about 3 per cent. higher than that of the summer variety. Williams finds the water-content of the plaice (*Pleuronectes platessa*) to be 79.86 per cent., while in the report of the U. S. Commissioner of Fish and Fisheries the value for the same fish is 77.39 per cent. The government analyst also reports 85.04 per cent. of water for the summer flounder and 84.35 per cent. for the winter

flounder (*Pleuronectes americanus*). It will be seen that the government figures accord neither with Williams' nor our own. The government values are based upon the analysis of but one fish in each case. Ulrich did not analyze a fresh specimen, but reports the water-content of smoked flounder to be 71.66 per cent.

On comparing the results for the three series, it will be noted that there was practically no change in the water-content. This would be naturally expected, because of the care taken to keep the fish completely encased in ice during the storage period. In the case of beef, however, Emmett and Grindley<sup>15</sup> report a loss of 1.3 per cent. of moisture after a forty-three days' period of storage.

**Total solids.** As the value for total solids was determined by difference, it varied inversely as the water-content. Our results show that there was no change in the water-content. Consequently, the value for total solids remained unchanged.

**Inorganic matter.** There was no reason to believe that possible changes in the flesh during cold-storage would affect the ash-yield, yet for an adequate analysis of the fresh specimen it was desirable to make this determination. By repeating the determination on the cold-stored products we were able to obtain a closer value for the ash-yield and at the same time detect any unexpected change. Ash determinations were made only upon summer flounders. The government analyst in the report already quoted gives the following percentage values for the ash content of three related fish: summer flounder, 1.29; winter flounder, 1.20; and plaice, 1.46. As was expected, the results obtained by us showed that cold-storage was without effect on the yield of ash.

**Organic matter.** As in the case of total solids, organic matter was determined by difference. Its variations were dependent upon variations in water-content and ash-yield. There being practically no variations in these, the percentage of organic matter remained unchanged.

**Ammonium nitrogen.** Without doubt this was our most important determination, especially from the standpoint of detection of bacterial influences. Our method, as already described, differs from that used by Pennington and Greenlee<sup>16</sup> in that we substituted

<sup>15</sup> Emmett and Grindley: *J. Ind. Eng. Chem.*, 1909, i, p. 413.

<sup>16</sup> Pennington and Greenlee: *Journ. Am. Chem. Soc.*, 1911, xxxii, p. 561.

sodium hydroxid for sodium carbonate. After a long series of experiments, Pennington and Greenlee found that the results obtained with the modified Folin method agreed very well with those obtained when the older magnesium oxid method was used. By using sodium hydroxid we were open to the criticism that our results might be higher than actual ammonium values. Yet granting this possibility, we found that the proportion of ammonium nitrogen was very low, even after a nine months' period of storage. If, therefore, by using a method which might give high results, no increase in ammonium nitrogen was found, after six months of storage and only a trivial increase after nine months of storage, it is fair to conclude that the fish were practically unchanged at the end of the last named period of storage. [See the preceding paper by Shulansky and Gies (p. 45) and the succeeding one by Perlzweig and Gies (p. 69).]

Pennington and Greenlee found the ammonium nitrogen content of *fresh* chicken meat to be 0.012 per cent. Houghton<sup>17</sup> reports 0.021 per cent. of ammonium nitrogen in *fresh* light chicken meat and 0.039 per cent. in the same kind of meat after a period of *five months of storage*. For dark chicken meat he reports 0.019 per cent. ammonium nitrogen in the *fresh* sample and 0.026 per cent. after a period of *five months of storage*. It would appear, then, that so far as the production of ammonium nitrogen is concerned, fish in cold-storage change more slowly than chickens.

**Total nitrogen.** Unless some ammonia was formed in the fish, and escaped into the air, there would be no chance for any diminution in the nitrogen content. Total nitrogen remained unchanged. It will be noticed that there is a difference of about 1 per cent. between the nitrogen content of flukes and flounders. This variation is partly explained when one takes into consideration the difference in contents of water.

**"Soluble nitrogen."** If any hydrolytic changes took place during the cold-storage period it would be natural to suppose that one or more of the nitrogenous constituents of the muscle became more soluble, or, in other words, that there was an increase in the "soluble nitrogen." Our results indicate that there was no in-

<sup>17</sup> Houghton: *J. Ind. Eng. Chem.*, 1911, iii, p. 497.

creased solubility of nitrogeneous substances. In the case of chicken, Houghton reports a slight increase in "soluble nitrogen" for light meat and a slight decrease for dark meat.

**"Coagulable nitrogen" and "non-coagulable nitrogen."** From the data in the tables it appears that there was a very slight increase in "coagulable nitrogen" and a corresponding decrease in "non-coagulable nitrogen." These differences are too slight to warrant any inferences.

**Lipins.** The term lipins is used to indicate the fats and fat-like substances in the "ethereal extract."<sup>18</sup> The flesh of the winter flounders that were used for the determinations was comparatively poor in ether-soluble constituents. The actual weight of lipins neutralized at any time was always less than one gram. This admits of relatively large degrees of experimental error; according to Allen,<sup>19</sup> 5 to 50 gm. of material should be used for this determination. Other authors recommend at least 4-5 gm. In our work such large samples were not available. While the values here reported are possibly somewhat too high, it is significant that there is no increase in acidity during a nine months' period of storage.

It is difficult to believe that the lipins would undergo any changes, significant of deterioration in nutritive value, which would not be shown more strikingly by the protein constituents of the flesh. The negative findings in this particular connection accord with such a view of the matter.

**Reducing substances.** We determined the reducing power of aqueous extracts, in order to detect any sugar which might have resulted from the hydrolysis of glycogen during the cold-storage period. A similar determination was made by Williams,<sup>20</sup> but her method involved the hydrolysis of all carbohydrate-yielding substances. She treated fish-powder with boiling dilute hydrochloric acid solution under a reflux condenser for three hours; proteins were removed by precipitation with lead acetate; then, after removal of the excess of lead, the reducing power of the filtrate was determined by the Fehling method and reported as percent. of glucose.

<sup>18</sup> Rosenbloom and Gies: *BIOCHEMICAL BULLETIN*, 1911, i, p. 51.

<sup>19</sup> Allen: *Com. Organic Anal.* (3 ed.), Vol. 2, pt. 1, p. 105.

<sup>20</sup> Williams: *Trans. Chem. Soc.*, 1897, lxxi, p. 651.

By this method a reducing power of 2.32 per cent. was reported for the plaice (*Pleuronectes platessa*).

Our own method failed to show any reducing power. Artificial hydrolysis was avoided. We were unable to get satisfactory responses to our qualitative tests for the presence of sugar in protein-free extracts, both from fresh and storage fish. For a comparative test, glucose, to the amount of 0.01 per cent., was added to one of the extracts, and a characteristic reduction obtained. For the quantitative determination of small amounts of sugar in meat, Bauer<sup>21</sup> recommends a spectroscopic method, since the polarimetric and titrimetric processes are unreliable for amounts less than 0.5 per cent. As no sugar was detected qualitatively, either before or after cold-storage, it seemed quite certain that no appreciable hydrolysis of glycogen had taken place.

**Quantitative reaction of aqueous extracts.** The reaction of aqueous extracts was always found to be acid to both litmus and phenolphthalein. From the data in the tables it is evident that the acidity of the aqueous extract was not materially affected by long periods of cold-storage. In several instances the same extract was titrated after standing for from two to four days in an ordinary house refrigerator. In each case the variation in acidity was within the limits of error of the method itself.

The general analytic results of our work are summarized in Table 4.

TABLE 4

*Summary of general average data*

Months in cold storage	Summer flounder (fluke)				Winter flounder.					
	Water	Nitrogen		Ash	Water	Nitrogen			Lipins	
		Total	Ammonium			Total	Soluble	Non-coagulable	Per cent	Acidity
	%	%	%	%	%	%	%	%		
None . . . . .	78.56	3.44	0.0195	1.28	81.75	2.89	0.964	0.383	0.379	136
Six . . . . .	78.69	3.33	0.0142	1.29	81.58	2.79	0.887	0.351	0.366	136
Nine . . . . .	78.45	3.40	0.0213	1.28	82.04	2.83	0.937	0.353	0.443	127

<sup>21</sup> Bauer: *Arb. a. d. kais. Gesundheitsmt*, 1908, xxx, p. 63.



## IV. SUMMARY OF CONCLUSIONS

1. The proportions of water in, and yield of ash from, the flesh of flounders were unaffected by a nine months' period of cold-storage.

2. The changes in the proportions of soluble, coagulable and non-coagulable nitrogenous constituents were negligible.

3. During a nine months' period of cold-storage, there was practically no change in the content of ammonium nitrogen.

4. For fish with a low content of lipins, there was apparently no increase in the acidity of the muscle lipins during a nine months' period of cold-storage.

5. There was no production of reducing substance from any constituent of the flesh during any of the storage periods.

6. There was no evidence, whatever, of any depreciation in the nutritive value, or any change in the sanitary character, of the fish at any time during nine months of cold-storage.

The writer wishes to record his indebtedness and to express his thanks to Prof. William J. Gies under whose direction this work was done.<sup>22</sup>

<sup>22</sup> See the succeeding paper by Perlzweig and Gies (p. 69), for additional data on this subject.

# A FURTHER STUDY OF THE CHEMICAL COMPOSITION AND NUTRITIVE VALUE OF FISH SUBJECTED TO PROLONGED PERIODS OF COLD STORAGE

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The study described in the preceding paper<sup>1</sup> was interrupted in October, 1912, by Dr. Smith's appointment to his present position in the Bureau of Chemistry at Washington. It has given us pleasure to proceed with the work to the end of the second year of storage. As the experiments by Dr. Smith were conducted under the guidance of the senior author, it has been a simple matter to continue the study without deviation from the plans and procedures of the preliminary part of the work.

The methods of analysis, as well as the detailed conduct of the work, were strictly in accord with the descriptions at page 57 of Dr. Smith's paper. The *averages* of our analytic data are recorded in the accompanying table, which, for convenience of comparison, includes the analogous figures from Dr. Smith's table on page 67.

The data in the accompanying table indicate very clearly that the fish under examination did not undergo any chemical change of importance, from the standpoint of nutritive value, at any time during a storage period of two years.

General microscopic examination of the flesh indicated that there had been no material alteration of the fibers in any instance. Crystals of triple phosphate were never detected in or on any of the muscle fibers, a finding in accord with the data for ammonium nitrogen in the flesh. Kept in an ordinary refrigerator after their delivery to us, these fish, like fresh ones, appreciably deteriorated in a few days and crystals of ammonio-magnesium phosphate could then

<sup>1</sup> Smith: BIOCHEMICAL BULLETIN, 1913, iii, p. 54.

be detected in the flesh at all exposed surfaces. The whole fish and all portions of the flesh, in every instance (12 hours after thawing), were devoid of any odor that might have indicated significant bacterial change (comparisons were made with fresh fish of the same kind). The stomachs of the fish, even at the end of two years of

*General average data pertaining to the composition of flounders in cold storage*

*A. Average analytic data quoted from Smith's paper, p. 67 (Table 4)*

Months in cold storage	Summer flounder (fluke)				Winter flounder						
	Water	Nitrogen		Ash	Water	Nitrogen			Lipins		Reac- tion of aqueous extract†
		Total	Am- monium			Total	Soluble	Non-co- agulable	Per cent.	Acid- ity*	
0	%	%	%	%	%	%	%	%			
0	78.56	3.44	0.0195	1.28	81.75	2.89	0.964	0.383	0.379	136	1.37
6	78.69	3.33	0.0142	1.29	81.58	2.79	0.887	0.351	0.366	136	1.17
9	78.45	3.40	0.0213	1.28	82.04	2.83	0.937	0.353	0.443	127	1.23

*B. Averages of our own analytic data*

17	78.91	3.46	0.0177	1.23	.....	.....	.....	.....	.....	.....	.....
20	.....	.....	.....	.....	79.14	.....	.....	.....	0.411	134	1.28
21	79.24	3.51	0.0205	1.26	.....	.....	.....	.....	.....	.....	.....
22	.....	.....	.....	.....	76.93	3.39	0.876	0.433	.....	.....	1.20
23	79.19	3.26	0.0231	1.25	81.26	.....	.....	.....	0.301	147	.....
24	75.74	3.28	0.0217	.....	76.32	3.55	1.008	0.379	.....	.....	1.32

storage, sometimes contained large masses of undigested matter—in a number of instances small fish that had been swallowed were almost wholly undigested!<sup>2</sup> The gastric and intestinal membranes were intact, and withstood a surprising degree of tension. The abdominal viscera in general were sound and, when handled, emitted no odor that is not common to them when exposed in fresh flounders.

The constancy in the data for the yield of ammonium nitrogen,

\* Expressed as mg. of KOH required to neutralize 1 gm. of the total lipin mixture.

† Expressed as c.c. of  $n/5$  NaOH sol. required to neutralize 100 c.c. of extract. These data for the first three records (A) were compiled from Tables 1-3 in Dr. Smith's paper.

<sup>2</sup> In one case, 2 years and 19 days after the flounder was sent to storage, the stomach contained two fishes, each of which was about 5 in. long and  $1\frac{1}{4}$  in. wide at the middle of the body. Digestion was advanced at the caudal end of one of these fishes, in the abdominal region of the other, and it was apparent that digestion of the skin had occurred here and there, but it was surprising to note how little change had occurred. There was no putrefactive odor.

for the reaction of the aqueous extracts, and for acidity of the lipins, show conclusively that there was no appreciable alteration of the flesh of the fish through *bacterial* influences. The uniformity in the data for "soluble" and for "non-coagulable" nitrogen (making due allowance for the gradual loss of water from most of the fish as the storage period lengthened) shows that there were no appreciable *autolytic* changes.

Some of the fish that had been subjected to analysis, including three in storage for *two years*, were served with meals in conventional ways to a number of people, the authors among them. These portions were palatable and entirely acceptable. The taste was slightly different, perhaps somewhat more "fishy," though not unpleasantly so, but otherwise there was nothing to suggest a lack of freshness.

The data in Dr. Smith's paper and this one pertain to flounders that were sent to cold storage *very soon after the fish had been caught*. These fish were not removed from cold storage before our order was given for their shipment to this laboratory. They were delivered within an hour afterward, and analysis was begun within 12 hours after their delivery to us.

We do not suggest that our findings would apply in any degree to fish that were not strictly fresh and unspoiled before they were put in cold storage. It is obvious, also, that these results have no bearing on the condition of fish which have been removed from cold storage and kept a week or more in a shop, exposed, until sold, to public inspection during market hours, and iced or kept in a common refrigerator at night. It is equally obvious that these data have no material bearing on the cold storage of anything except fish.

The results of our studies convince us that fresh fish, similar in general character to flounders, may be preserved frozen, by the best cold storage processes, for at least two years without undergoing any important chemical alteration, and without materially depreciating in nutritive value.

## THE INFLUENCE OF CHRONIC UNDERNUTRITION ON METABOLISM

Prof. N. Zuntz recently reported<sup>1</sup> the results of an investigation which the writer of this note undertook under his personal guidance at the Tierphysiologisches Institut, Berlin, and which was later continued by Dr. Diakow of St. Petersburg.

The subject of these experiments, a female mongrel weighing 10 kg., had been kept on a controlled diet (150 gm. of horse meat and 80 gm. of rice) for nearly a month, during which period three respiration experiments were performed with the Regnault-Reiset apparatus. Although the food was not quite sufficient to completely cover the energy requirement of this dog, the latter had been putting on nitrogen, but towards the end of the preliminary period a state of equilibrium was attained.

Beginning February 23, 1912, the diet had been considerably reduced (60 gm. of meat and 35 gm. of rice) and for over a year, until the animal's death, it remained below the actual need of the organism.

A respiration experiment, performed about three weeks after the insufficient feeding had been begun, showed a shortage of 220 cal. per day, which had been drawn from the dog's substance. Considering that, as the nitrogen determination in the urines showed, only 7.5 cal. had been derived from the protein material (corresponding to 9 gm. of flesh), the remaining 212.5 cal. must have been furnished by 22.4 gm. from the fat depot of the organism. The total metabolism had changed, in the meantime, from 553 cal. to 394 cal. per day.

The limits of this review will not permit discussion of each experiment. The average number of cal. liberated by our dog, in the course of the subsequent six weeks, was 149 cal. in excess of the supply per day. As there had been very little loss of nitrogen, it may be assumed that all the extra energy was derived from body

<sup>1</sup> Zuntz (Versuche von S. Morgulis and M. Diakow), Einfluss chronischer Unternährung auf den Stoffwechsel: *Biochemische Zeitschrift*, 1913, lv, p. 341.



fat, in which case a loss of 770 gm. should have been occasioned. In other words, the body weight would have changed from 7.53 kg. to 6.76 kg.; the weight actually observed at that time was 6.96 kg. Likewise, on the 20th of July, when the body weight had diminished to 6.36 kg., the observed loss fully agreed with the expectation based upon results of the respiration experiments.

After I left Berlin, the dog was maintained on the same diet and, in January 1913, my colleague, Dr. Diakow, continued the series of experiments which had been begun a year ago. In the concluding period of 82 days, *i. e.*, until the animal died, Dr. Diakow performed five respiration experiments. The excess of energy produced has been 117 cal. per day, which is equivalent to 11.7 gm. of fat. Since 1,400 gm. were lost during that period, or 17.1 gm. per day, it is evident that some of that energy must have been derived from protein. Unfortunately, Dr. Diakow made no determinations of the total nitrogen in the food and in the urines, but Professor Zuntz computes that an average of at least 0.2 gm. must have been lost daily.

The most remarkable fact in connection with the second part of this research is the rise in the energy requirement which, in spite of the fact that the body temperature was very low, increased to the same level as before the underfeeding. Professor Zuntz's conjecture that this rise in the metabolism was coincident with an increased nitrogen elimination, as the fat was being exhausted, is entirely borne out by the results of my recent unpublished work on the metabolism of chronic underfeeding wherein this matter has been studied from a much wider point of view.

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## NITROGEN METABOLISM DURING CHRONIC UNDERFEEDING AND SUBSEQUENT REALIMENTATION

In the course of an extended physiological investigation of the effects of chronic underfeeding, a number of observations on the nitrogen metabolism have been made which will be briefly discussed in this *preliminary note*.

The experiments were made with a dog weighing 14 kg. The animal was fed a very liberal, but not excessive, diet for ten days. During this time it was found that 78.7 percent of the absorbed nitrogen had been eliminated by the kidneys. The quantity of food was then reduced to one-third, so that in the course of several weeks the dog was obliged to live at the expense of its own tissues. The amount of nitrogen in the food was very low, which circumstance caused a continuous waste of the nitrogenous material of the body. Correspondingly, the nitrogen eliminated in the urine for the first week of underfeeding was 85.4 percent above the amount actually absorbed.

The supply of nitrogen during the period of chronic starvation varied from 21.7 to 23.1 gm., per week. The nitrogen elimination remained very uniform until a late period in the experiment, when quite abruptly it increased about 25 percent. This increased nitrogen elimination coincided with a series of interesting changes in the animal which cannot, however, be alluded to here. It was occasioned by a greater combustion of protein, due to the exhaustion of the fat of the body. The specific gravity of the daily urines throws some light on this matter. The average sp. gr. of the normal urine was 1.0141, while during the early part of the underfeeding it was 1.0124. In the concluding two weeks the sp. gr. rose to 1.0186 (the volume being practically the same), owing to the liberation of inorganic substances by the protein decomposition. The study of the gaseous exchange and the respiratory quotients furnished further unequivocal proof that the organism derived its energy from the oxidation of the muscular substance.

After the animal's weight had diminished over 40 percent, and its physical strength had been reduced to such an extent that it was unable to enter its cage but had to be lifted into it, the dog was again given a rich diet; and in four weeks time it fully recovered the

original weight. The general physiological transformation of the animal during that short time has been studied carefully and will be related in detail when the entire work is published.

Nitrogen was avariciously retained by the organism during realimentation, so that in these four weeks the organism was enriched by 191 gm. of protein after it reclaimed what had been lost during the chronic underfeeding. In the first week only 58 percent of the absorbed nitrogen appeared in the urines, but this relation gradually changed; and as early as the fourth week, 73.8 percent was eliminated, or nearly as much as for the preliminary period.

With the resumption of feeding a striking change occurred in the reaction of the urine. The urines were tested every day and were invariably acid to litmus paper. On the third day of refeeding with superabundant quantities of food, it was observed that the urine lost its clearness, having become strongly alkaline. It seemed at first that the alkalinity was caused by bacterial contamination, but preservation of the urine with thymol over night did not prevent its being alkaline. There was no indication of disease in the dog, although persistent alkalinity of the urine is generally regarded as a symptom of cystitis. The alkalinity was due to an excess of ammonium carbonate in the urine, as could be shown by a very simple experiment. Two different strips of litmus paper were dipped in the urine, whereupon the red became dark blue, but the blue strip remained unaffected. The two strips were then allowed to dry, when the red color was restored to the former and the latter turned red. The strong ammoniacal smell of the urines left no doubt as to the true cause of the alkalinity. This condition lasted for only a few days, when the urines cleared up again; and the normal acid reaction returned, and remained undiminished thereafter. Unfortunately, I was unable to study the nitrogen partition, but I would venture to suggest that the great influx of phosphates and acid cleavage products of the protein digestion, coupled with a generally impaired condition of the liver and of the whole organism, for that matter, resulted in a rapid elimination of ammonium carbonate before its transformation into urea.

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PROCEEDINGS OF THE BIOLOGICAL SECTION OF  
THE AMERICAN CHEMICAL SOCIETY,  
ROCHESTER, NEW YORK,  
SEPTEMBER 10-12, 1913

I. EXECUTIVE PROCEEDINGS

The Section met with the secretary acting as the chairman at the session of the first day. Announcements were made to the effect that the chairman, Dr. C. L. Alsberg, was in attendance at the meeting of the American Public Health Association, at Colorado Springs and hence would not be present at the first day's session of the Section; that the Council of the Society had approved the by-laws as proposed by the committee for the proposed formation of the Section into a Division;<sup>1</sup> that a copy of the by-laws, which would be presented for consideration and final action at the last session, was available for inspection; and that a nominating committee consisting of P. Rudnick, M. X. Sullivan, and P. A. Kober had been appointed. The Section then proceeded with the reading of papers, of which abstracts are given on pages 80-95.

Following the reading of papers, the chairman addressed the Section. (See page 77.)

The session closed with the business meeting. The by-laws, as recommended by the committee and approved by the council, were unanimously adopted. The nominating committee reported their recommendations: *Chairman*, C. L. Alsberg; *vice-chairman* and *secretary*, I. K. Phelps; *members of the executive committee*—W. D. Bancroft, chairman, Edward Kremers, A. W. Dox, A. D. Emmett, and D. D. Van Slyke. The gentlemen nominated were unanimously elected the officers for the ensuing year. The secretary read a statement drawn up by W. A. Noyes concerning the advisability of the Division taking some action toward securing a special journal restricted to organic and biological papers, and pub-

<sup>1</sup> Alsberg: BIOCHEMICAL BULLETIN, 1911, i, p. 94.

lished by the society. Considerable interest in the possibility of such a journal was shown, but, as no practical method of financing the project was presented, no action was taken.

I. K. PHELPS, *Secretary*.

*Bureau of Chemistry,  
U. S. Department of Agriculture,  
Washington, D. C.*

## II. CHAIRMAN'S ADDRESS, SEPTEMBER 12, 1913

Gentlemen, I did not come to Rochester with the intention of making a speech, but find—I am sorry to say—that Professor Chambers expects me to talk. He made the request—or, shall I say, demand—as we came into this room. I find that I am driven to the usual refuge of those who have to speak when they would rather be silent—that is, I will take refuge in the history of my subject.

This subject has, I think, some general interest because originally no very definite distinction was made between biochemistry and any other kind of chemistry. One of the first real biochemists was Lavoisier, whom all matter, whether living or dead, interested. He performed the first calorimetric experiments. He was the inventor of the ice calorimeter, and showed that animal heat was the result of oxidation. All the chemists of that generation and the immediately succeeding one did biochemical work. I need only cite Liebig, who is perhaps in some ways the greatest of all biochemists. Unfortunately, about the latter part of Liebig's life chemists lost interest in biochemistry. This was due very largely to the sudden and tremendous development of organic chemistry, which was brought about by the discoveries of men like Hofmann and Kekulé. It was so easy to make new synthetic substances and, thereby, gain a sort of immortality, even though the main result of putting a chlorine atom here and a bromine atom there was to fill up Beilstein. In consequence, thoroughly trained chemists did not busy themselves with subjects that were really important in the elucidation of that matter which is found in living organisms, and which forms the physiological basis of life. The scientists in biology and medicine needed such information. The chemists did not give it to them. Consequently, physicians and physiologists who were ill-equipped for chemical research were forced to carry forward the work of



biochemistry. Though the net result of their work made decidedly for progress, only too often it created confusion and artificial difficulties. Even the best biochemists of those days make us wonder why they did not pursue their chemical investigations as far as the chemical methods of that day would permit. The answer is, I think, in many cases, that they were not real chemists but physiologists with a chemical veneer. Fortunately, this has been changing during the past decade, largely owing to the work of Emil Fischer. While we recognize in him a master of chemical technique, we may be certain that in a measure, at any rate, the preeminent position which he occupies among the chemists of his time is due to his clear conception of the really most important work in organic chemistry along biochemical lines. Fortunately, more and more organic chemists are following in his footsteps, and are devoting their attention to substances which occur in living things.

I wish here to make a plea for more of this sort of work in America. I believe that the rewards and recognition for knowledge of chemistry applied in biochemistry are great, because the work of the biochemist will be applauded not merely by chemists, but also by zoologists, botanists and physicians. A biochemist has a wider audience because his work presents a more general appeal than the work of organic chemists upon such subjects as dye-stuffs and the like.

Further, I wish to point out the value of instruction in allied subjects. Not every organic chemist can successfully attack all biochemical problems. Besides his organic chemistry, other experience in physiology and, above all, experience in dealing with substances which do not crystallize, is necessary. In many cases it is difficult to conduct biochemical research because the biochemist must very frequently begin with the smears which the organic chemist consigns preferably to the slop jar. While the things which will not crystallize interest less the organic chemist, they are the very classes of substances with which the biochemist must deal. Great care, great patience and a knowledge of colloids are required of the organic chemist who wishes to work in biochemistry, but I feel confident that the reward for such men is great, not merely in pure science, but also in industries and in the arts.

The history of biochemistry in America is similar to that abroad. In America it developed first in the seventies and eighties in the medical schools of the country; and, at that time, it was controlled by physicians and physiologists abroad. The subject was narrowed to the consideration of biochemistry as affecting the life of man; that is to say, the chemical side of physiological processes of the human body together with such considerations of bacteriological chemistry as affect man in health and in disease. This phase of biochemistry is cared for very adequately and acceptably by the American Society of Biological Chemists, the first biochemical society to be formed in America.

The phases of biochemistry which the American Chemical Society can very naturally expect to encourage are quite distinct from the aims of the American Society of Biological Chemists. Our usefulness will include the biochemistry affecting agriculture, phytochemistry, in particular, and such industrial processes as are based upon biochemical reactions; for example, the more exact study of the chemical composition of fruits, grains, and food products. It must be admitted that, at present, we know only those chemical substances occurring in considerable amounts in such important grains as wheat and corn. The minor constituents in grains of much importance have not been identified with exactness. If we consider grains of less importance, even this degree of knowledge can not be claimed.

Some of our most important modern industries, like those dealing with starch, artificial fabrics, leather, tanning materials, glue and gelatin, meat packing and the flour milling industry require biochemists, and we are now training men to deal with such practical problems.

If our society confines itself to the activities already mentioned, there still remains a wide field of biochemistry uncared for: the biochemistry of the lower animals. This part of the biochemical work will become a part of the work in the zoological societies of the country.

My view is that three societies of biological chemistry can well exist in America without competing in any way, and each one caring for a specific need. These would include the biochemistry of

the higher animals and its application to medicine; the biochemistry of the lower animals; and biochemistry in its application to plants, agriculture, and the industries.

CARL L. ALSBERG, *Chairman*

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### III. SCIENTIFIC PROCEEDINGS (ABSTRACTS)

**On the presence of histidine-like substances in the pituitary gland (posterior lobe).** T. B. ALDRICH. (*Research Laboratory of Parke, Davis & Co., Detroit, Mich.*) Employing Pauly's diazobenzene sulphonic acid reaction for the detection of histidine, it seems probable that histidine or some form of it is contained in a free state in the desiccated posterior lobe of the pituitary gland since, by benzoylating direct, using Inouye's method, Pauly's reaction was positive. The substance (or substances) giving Pauly's reaction, after hydrolysis by means of mineral acids or digestion with pancreatin, is not tyrosine (which gives a similar reaction) since, after benzoylating, the histidine reaction still persists. Furthermore, the histidine-like substance (or substances) is probably not histidine, since it does not give Weidel's reaction as modified by Fischer, or Knopp's reaction with bromine. It is probable, also, that Pauly's reaction is not a specific reaction for histidine.

**The mutual action of pepsin and trypsin.** J. H. LONG. (*Northwestern University Medical School, Chicago.*) The earlier physiologists seem to have considered this a comparatively simple question, but their findings were not in agreement. Kühne was one of the first to discuss the problem and he concluded that pepsin destroys trypsin. This is probably correct but his experimental evidence does not warrant the statement. In all such experiments the reaction of the medium must be definitely known as the concentration of hydrogen or hydroxyl ions is often the determining factor. In most of the earlier work these points were almost wholly overlooked, as the combining power of protein for acid or alkali was either not known or not recognized. Making due allowance for the reaction of the medium, the present experiments show that, within the practical limits of behavior in the body, trypsin has no important

action on pepsin, whereas the action of pepsin on trypsin is markedly destructive. While an acid medium weakens trypsin, pepsin plus acid seems to destroy it rapidly.

**A further study of the well water of Delaware, Ohio.** G. O. HIGLEY. (*Ohio Wesleyan University, Delaware, O.*) This study was intended to supplement the report made at the spring meeting: to trace the relation between well water and an outbreak of typhoid. The city water has been examined and found safe. The water of about 100 wells has been analyzed and much of it found polluted. Five vaults were selected in various parts of the city and in markedly different soils: these were heavily salted and a weekly test for chlorides made during a period of nearly two months, in the water of thirteen wells located from 58 to 118 feet from the vaults. Comparison of results of analyses, made before and after the salting process, showed a decided increase in chlorides in the well water at four of the five centers and in seven of the thirteen wells.

**On the distribution of mercury following acute bichloride of mercury poisoning.** JACOB ROSENBLUM. (*Biochemical Laboratory of the Western Pennsylvania Hospital, Pittsburgh, Pa.*) Estimations of the amount of mercury in the organs of a woman who died 8 days after ingestion of bichloride of mercury.

**The non-interference of ptomaines with certain tests for morphine.** JACOB ROSENBLUM and S. ROY MILLS. (*Biochemical Laboratory of the Western Pennsylvania Hospital, Pittsburgh, Pa.*) We have determined experimentally that bacterial products, formed during aerobic and anaerobic putrefaction of various human organs, do not give reactions simulating those due to the presence of morphine. In no way do they interfere with the detection of morphine when the latter is added to a mixture of these putrefactive products.

**The effect of electrolysis on whole proteins, Witte peptone, and some of their decomposition products.** JAMES P. ATKINSON. (*Chemical Laboratory, Department of Health, City of New York.*) Whole protein (egg white), Witte peptone, and protein (horse serum) hydrolyzed by hydrochloric acid, yield approximately 50 percent of the total nitrogen as ammonia, when electrolyzed in a sulfuric acid solution. The amino acids tested, glycylglycine, uric acid and urea, do not yield as much nitrogen in the



form of ammonia under the same conditions. Ammonium sulfate is unaffected.

**The non-development of cytolytic sera following the intravenous injection of mould spores.** A. F. BLAKESLEE and R. A. GORTNER. (*The Carnegie Institution of Washington.*) Intravenous injections of the spores of each race of *Mucor* "V" were given to rabbits, rabbit No. 5 receiving 30 injections of the ♂ race and rabbit No. 55 receiving 29 injections of the ♀ race. Each injection averaged about 500,000,000 spores. Following the last injection of approximately 800,000,000 spores, a loop of blood was taken at intervals of 30 minutes for 6 hours, then every hour for 4 hours more, then every 2 hours for 16 hours more, and later at less frequent intervals. Separation cultures were made of agar which contained the loop of blood taken and the number of mould colonies which developed were counted. A similar test was made at the same time, using rabbits which had received their first injection of the spores. In each case the disappearance of the spores occurred after about 43 hours, the immunized rabbits retaining the viable spores as long as the control rabbits.

**Effect of acids upon the catalase of taka-diastrase.** RAY E. NEIDIG. (*Chemical Section of the Iowa Agricultural Experiment Station, Ames.*) Data were presented showing the inhibiting effect of several of the important inorganic and organic acids on the action of the catalase of taka-diastrase. Curves were plotted, for different acid concentrations, which show the quantity of oxygen liberated at stated intervals. The acids, arranged in order of the magnitude of their inhibiting effect for equi-normal solutions, are as follows: sulfuric, hydrochloric, oxalic, tartaric, citric and acetic. The inhibiting effect of the first three was much more pronounced than that of the others. Neutralization of the acid solution usually restored some of the activity, the amount of increase depending upon the particular acid used. Van Slyke's amino-nitrogen apparatus was used in these experiments for measuring the amount of oxygen liberated.

**Polyatomic alcohols as sources of carbon for molds.**<sup>2</sup> RAY E. NEIDIG. (*Chemical Section of the Iowa Agricultural Experi-*

<sup>2</sup> Neidig: *Jour. Biol. Chem.*, 1913, xvi, p. 143.



ment Station, Ames.) A comparison of some of the polyatomic alcohols occurring in nature was undertaken in order to determine the degree of their utilization by molds as sole sources of carbon. The alcohols used were methyl alcohol, glycol, glycerol, erythrite, adonite, mannite, dulcitol and sorbitol. Eight species of molds representing four genera were cultivated in media containing these alcohols. It was found that methyl alcohol produced no growth, glycol induced germination only, glycerol produced strong cultures, erythrite was utilized by the majority of molds and adonite by only a few, while all three of the hexatomic alcohols may be regarded as good sources of carbon. These results indicate that molds are able to use both optically active and inactive compounds as sources of carbon. If viewed from the standpoint of their oxidation products, it is possible that active compounds are first formed and these are then utilized in the development of the molds.

**Cleavage of benzoylalanine by mold enzymes.** ARTHUR W. DOX and W. E. RUTH. (*Chemical Section of the Iowa Agricultural Experiment Station, Ames.*) See page 23.

**Influence of certain organic substances upon the secretion of diastase by various fungi.** CHRISTINE CHAPMAN and W. C. ETHERIDGE. (*Laboratory of Plant Physiology, State College of Agriculture, Cornell University, Ithaca, N. Y.*) In this work the influence of varying concentration of cane sugar, glucose, peptone and tannic acid upon the secretion of diastase by *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium expansum*, *Penicillium camembertii*, *Mucor Rouxii* and *Cephalothecium roseum* has been investigated. Czapek's solution was employed with the sugar replaced by 0.4 per cent soluble starch. To this was added the substance whose influence was to be determined. It was found in general that the presence of any of these organic substances retarded the secretion of diastase by the fungi mentioned. The higher the concentration the greater the retardation.

**A method for studying slight degrees of glycosuria, adapted from Macleod and S. R. Benedict.** AMOS W. PETERS and MARY E. TURNBULL. (*Biochemical Laboratory, Training School for Feeble-minded Children, Vineland, N. J.*) Urine is clarified by the method of Macleod, *i. e.*, urine + concentrated acetic acid +

Merck's blood charcoal. No sugar is lost by this procedure. If the urine is diluted to only 7/5 original volume, the filtrate is water-clear for polarization. Of the filtrate, 5 c.c. are transferred to a 100 c.c. Kjeldahl flask, neutralized with a saturated solution of sodium carbonate, using alizarine as the indicator, and 5 c.c. of a modified Benedict reagent are added. After placing a pebble in the liquid and fixing the flask in an inclined position directly over a small Bunsen flame, the whole is boiled for  $2\frac{1}{2}$  minutes. The resulting small volume is transferred to a centrifuge tube and made up to 10 c.c. Examined under a shaded electric light and against a dark background, even a trace of glucose shows turbidity and after centrifugation as little as 0.0035 percent shows a film of red precipitate. Quantitative estimations are made by comparison with standards based upon a normal urine excreted on a normal diet and showing zero rotation (or nearly so) after clarification, and to which glucose is added in amounts that increase the content by successive increments of 0.01 percent. The sensitiveness is so great that such slight differences in proportion may easily be detected.

Composition of the modified Benedict reagent: sodium citrate, 100 gm.; sodium acetate, 100 gm.; sodium carbonate (anhyd.), 50 gm.; cryst. copper sulfate (Kahl.), 12.5 gm.; water (dist.), 500 c.c.

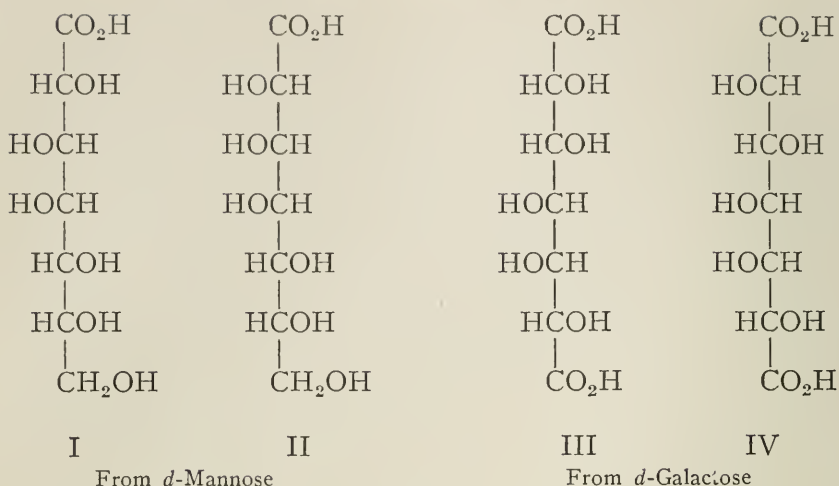
**The estimation of protein and amino- and nucleic-acids in potable waters.** PHILIP A. KOBER. (*Harriman Research Laboratory, Roosevelt Hospital, New York.*) Experiments show that by using the right precipitants and evaporating to one-tenth of the original volume, proteins and nucleic acids can be estimated in potable waters by the author's nephelometric method. This method will easily reveal the presence of one part of substance in one million parts of water. By using the copper method,<sup>3</sup> potable waters may be analyzed for amino-acid nitrogen before or after hydrolysis. This method will reveal one part of amino-acid nitrogen in one million of water, without difficulty.

**The fate of protein digestion products in the body.** DONALD D. VAN SLYKE and GUSTAVE M. MEYER. (*Rockefeller Institute for Medical Research, New York.*) Previous work by the authors

<sup>3</sup> Kober: *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 1546.

has shown that during digestion amino acids are absorbed into the blood, as the amino-acid nitrogen of the latter, per 100 c.c., rises, in a dog, from 4-5 mg. before feeding to 10-12 mg. after a meal of meat. The low concentration of amino acids in the blood even at its maximum indicates that the digestive products must be removed rapidly from the circulation. This is found to be the case after the injection of amino acids directly into the circulation. They disappear from the blood almost as fast as they enter it. Analysis of the tissues shows that these have absorbed the amino acids from the blood, without subjecting them to any immediate chemical change. This apparently follows later, but in the muscles the change is so slow that no decrease in amino-acid nitrogen can be determined within the first 3-4 hours after the injection. In the liver, on the other hand, the amino acids absorbed as the result of the injection have entirely disappeared by this time, indicating that the metabolism of these products is particularly rapid in the liver. It is less so in the other organs, but whether as sluggish as in the muscles is not yet certain. During starvation the amino nitrogen of the tissues, which amounts to 40-80 mg. per 100 g. of fresh tissue, tends to increase rather than disappear, indicating that the amino acids of the tissues can originate from autolysis of the tissues themselves as well as from digestion of food proteins.

**The configuration of some heptoses.** GEORGE PEIRCE. (*Laboratory of Pharmacology and Toxicology, University of Wisconsin.*) *d*- $\alpha$ -Mannohexahydroxyheptoic acid and *d*- $\alpha$ -galahexahydroxyheptoic acid yield, on oxidation, two pentahydroxypimelic acids that are optical antipodes of each other. The configuration of four of the asymmetric carbon atoms in each monobasic acid is known and the configuration of the fifth is indicated by the above fact. The corresponding heptites are also optical antipodes. Of the four configurations on page 86, I and III are seen to be the two that give optical antipodes on oxidation or reduction of the end carbon atoms. These two are therefore the formulae for the  $\alpha$ -compounds. The  $\beta$ -galactose compounds of formula IV have been synthesized but the  $\beta$ -mannose compounds of formula II have not yet been prepared.



**Vanillin in wheat and its relation to soil.** M. X. SULLIVAN. (*Bureau of Soils, U. S. Dep't of Agriculture, Washington, D. C.*) By means of the sodium bisulphite aldehyde method, an aldehyde that smelled like vanillin, and gave vanillin color reactions, was found in the alcohol and ether extracts of ungerminated wheat seeds; in the roots, seeds, and tops of young wheat seedlings; in rotten wood; and in the water in which wheat had germinated and grown. Estimated quantitatively by Folin and Denis' colorimetric method, the amount in the ungerminated seed is small (several parts per million) but is considerably increased during germination and the early stages of growth. Treating the seed with 5 percent sulfuric acid solution also increased the amount of vanillin that could be extracted. The presence of vanillin in other plants was indicated. The vanillin of soil undoubtedly has its origin in part in vegetable debris and the growing plant.

**Some organic constituents of the culture solution and the mycelium of molds from soil.** M. X. SULLIVAN. (*Bureau of Soils, U. S. Dep't of Agriculture, Washington, D. C.*) Examination was made for the organic constituents of the dried mycelium of mixed mold cultures from soil and of *Penicillium glaucum* grown on Raulin's solution, and of the filtered solution after mold growth. In the mixed molds was found a large number of organic substances, many of which were subsequently detected in *P. glaucum*. In the



alcoholic soda extract of *P. glaucum* were found oleic and palmitic acids, a fatty acid melting at  $54^{\circ}$  C., a fatty acid, which appears to be elaidic acid, hypoxanthin, guanin, adenin, histidin, thymin and cholin. In the direct alcohol extract were found mannite, cholesterol, hypoxanthin, and cerebrosides. From mold grown on Raulin's solution plus peptone a small amount of guanidin was obtained. In the culture solution, after a number of weeks' growth, were found fatty acids, purin bases, a small quantity of a histidin-like substance, pentose sugar, unidentified aldehydes, etc. Many of these compounds have been found in soil and the conclusion is drawn that microorganisms, such as yeasts, bacteria and molds, play an important part in their formation.

**A method for the determination of small amounts of fat.** W. R. BLOOR. (*Laboratories of Chemistry of Queen's University, Kingston, Canada, and of Biological Chemistry of Washington University, St. Louis, Mo.*) The method consists essentially in extracting the fat from the tissue or liquid with an excess of alcohol-ether (25 percent ether), measuring an aliquot portion of the filtered extract into distilled water and determining the amount of fat by comparison of the cloudy suspension so obtained with a standard fat solution by the use of the nephelometer. The method has given good results with blood and milk.

**Nitrogenous hydrolytic products of several phosphatids.** C. G. MACARTHUR and G. NORBURY. (*University of Illinois.*) Sheep-brain kephalin, sheep-brain lecithin, ox-heart cuorin and ox-heart lecithin were prepared, purified, and then hydrolyzed in a dilute hydrochloric acid solution. In each case the fatty acid residue contained nitrogen, usually about one-sixth of the total. The filtrate nitrogen was separated by a special method into four fractions, representing (1) ammonia, (2) cholin or other basic compounds, (3) amino acids, or compounds not precipitated by platinum chloride but precipitated by mercuric acetate in a sodium carbonate solution, and (4) the filtrate from (3). The two lecithins contain about two-fifths of the nitrogen in form 2, while kephalin and cuorin contain practically none. In all of them, fraction 3 is large, varying from one-third to one-half.

**Fatty acids from kephalin.** L. V. BURTON and C. G. MAC-



ARTHUR. (*University of Illinois*.) The fatty acids obtained from hydrolyzing purified kephalin in a dilute hydrochloric acid solution were separated by the lead acetate method into the saturated and unsaturated fatty acids. The saturated-acid fraction represented about one-third of the total and was found to contain stearic and palmitic acids in the ratio of three to one. The unsaturated fatty acids were separated by the bromination method into clupanodonic, linolic and oleic acids. The amount of clupanodonic acid present was small—less than 2 percent. The linolic acid was found to represent about one-sixth, oleic acid about one-third, of the total fatty acids.

**A metabolism experiment with swine.** E. B. FORBES. (*Department of Nutrition, Ohio Agricultural Experiment Station, Wooster*.) The usual practical rations for swine contain an excess of acid over basic mineral elements. Urinary ammonia varies directly with this excess of mineral acid, provided the protein intake remains the same. Increased protein intake increases urinary ammonia. This excess of mineral acid in practical swine rations does not seem to affect calcium retention.

Water drinking causes the elimination of sodium and chlorin; abstinence from drinking leads to their retention. The feces may contain an abundance of sodium but are nearly free from chlorin. Potassium, magnesium and chlorin balances were usually positive, but were negative during periods of maximum intake, apparently through over-response in the way of protective elimination of the excess ingested.

Calcium retention was satisfactory only on rations including meat meal (containing considerable bone) and skim milk. Neither cereals nor soy beans furnish the calcium requisite for growth. An excess of magnesium over calcium caused loss of calcium with a ration of rice polish and wheat bran. The excess of magnesium over calcium in corn and in other practical rations does not appreciably restrict calcium retention. The important deficiencies of corn are, in order of magnitude, calcium, phosphorus, and nitrogen.

Creatinin elimination was entirely independent of food but varied in the same order as live weight, weight of dressed carcass, of flesh, of bones and of blood.

Soy beans, meat meal and skim milk increase the digestibility of the carbohydrates of the corn with which they are fed. Meat meal and skim milk increase the apparent digestibility of the fat, and decrease the digestibility of the crude fiber of the corn with which they are fed, the results being digestion coefficients of more than 100 and less than nothing.

**The acidity of normal urine.** HOWARD D. HASKINS. (*Laboratory of Physiology and Biochemistry, Western Reserve Medical College, Cleveland, O.*) Certain modifications of Henderson's method were suggested. Permanent color standards were proposed for the range of acidity determined by paranitrophenol. A report was made of a study of variations of acidity in 24 hour samples and in fractional samples, *i. e.*, the day's urine collected in five periods. No relation of concentration of urine to acidity was noted. The effect of diet was slight. Night urine was distinctly acid in 50 percent of the cases, and morning urine (breakfast to 11) was of very low acidity in 50 percent of the cases. Sweating seemed to have a marked effect in causing higher acidity.

**Sunlight and health.** WILDER D. BANCROFT. (*Cornell University, Ithaca, N. Y.*) It is usually considered that plenty of sunlight is beneficial to health but Woodruff considers it harmful, especially in the case of tuberculosis. This discrepancy becomes less serious if we consider how light acts. The primary action of light is to tend to eliminate the substance which absorbs it; the primary action is a destroying one. On the other hand we get a secondary effect with living matter, which is or may be a stimulating one. Strychnine is beneficial in small quantities and toxic in large ones. When studying the effect of light on organisms, one should differentiate the two effects.

**The nature of humus and its relation to plant life.** S. L. JODIDI. (*Office of Physiological and Fermentation Investigations, Bureau of Plant Industry, U. S. Dep't of Agriculture, Washington, D. C.*) See page 17.

**The importance of food accessories as shown by rat-feeding experiments.** F. C. COOK. (*Animal Physiological Laboratory, Bureau of Chemistry, U. S. Dep't of Agriculture, Washington, D. C.*) Twelve white rats were fed on a basal diet of protein, fat,

and carbohydrate, plus Röhmann's salt mixture, for a period of 80 days. Most of the rats lost weight during the last three weeks. To the basal ration during 35 days immediately following the 80 days on the basal diet alone, 5 c.c. of a solution of meat extract, plant extract, or whole milk, were alternately added, the nitrogen and sodium chloride of the three accessories being equal. When meat extract or milk was fed, a marked increase of weight was obtained. Eleven young white rats were fed for 35 days on a basal diet, plus one of the three accessories. The stimulating effect of milk as shown by Hopkins was noted. The meat extract also acted as a stimulant, while the plant extract showed little, if any, stimulating action. The milk and meat extract gave the biuret reaction and heavy precipitates with phosphotungstic acid, but the plant extract did not give either of these reactions. The meat extract, which is a hydrolyzed product practically free from fat and carbohydrate, seems to possess the stimulating properties similar to milk, a natural product. That the calories are not the sole guide in feeding experiments, in harmony with the work of Hart, Hopkins, Osborne and Mendel, and others, was noted. The rats gained in weight on a smaller number of calories when milk or meat extract was ingested. No gain in weight was obtained with a larger number of calories in the food ingested in the absence of milk or meat extract.

**A time recorder for kymograph tracings.** OLIVER E. CLOSSON. (*Research Laboratory of Parke, Davis and Co., Detroit, Mich.*) It is at best a tedious operation to find the projection of the time record on the different graphs as ordinarily traced upon smoked paper. The time interval can easily be recorded by a fine line, entirely across the paper by the following simple device. A fine spring wire stretched two to three mm. from the smoked surface will strike the smoked paper on the rebound and remove a fine line of soot, when picked by the armature of the time-signal magnet. By a little adjustment, a single distinct line is recorded at each closure of the circuit. If it is inconvenient to adjust any recorder to write perpendicularly to the base line, it is a simple matter to make the adjustment so that the time line will be parallel to any such line.

**Apparatus for studying oxidases.** OLIVER E. CLOSSON. (*Re-*

search Laboratory of Parke, Davis and Co., Detroit, Mich.) As the reaction of oxidases with hydrogen peroxide liberates heat, the temperature factor as well as the expansion of the gas are very important and necessitate a thermostat control with continued agitation of the mixture for comparative studies.

To obtain uniform temperature and continuous record of the liberated gas, the following apparatus was devised. A shaking member with two compartments, one for holding the hydrogen peroxide and the other for the enzyme solution, is connected by a tube with ground joint to a large cylindrical container with its center at the axis of motion so that liquid in this container is not agitated by motion around the axis. This arrangement allows the shaking of the reacting solution and the measuring of the liberated oxygen by the water displaced. The large container has a tube extending along the axis to the outside of the thermostat, which allows the discharge of the displaced water into a vessel suspended by a spring, so that a writing arm can be made to record the volume, giving on a rotating drum a curve which can be analyzed at one's leisure.

**Surface tension in muscle contraction.** WILLIAM N. BERG. (*Washington, D. C.*) Macallum<sup>4</sup> quotes Jensen<sup>5</sup> to the effect that "a thread measuring 1 mm. in diameter formed of the plasmodium of *Chondrioderma*, a *Myxomycete*, may, when it is in the dense condition, bear up a weight of nearly a gram. If the force engaged is surface tension it would amount to about 6000 dynes per centimeter. . . ."

At the same time Macallum does not quote Pfeffer<sup>6</sup> who, in discussing the mechanics of ameboid movement says, that in the case of the plasmodium of *Chondrioderma*, the outer membrane may vary in its consistence from that of the fluid protoplasm in the interior of the cell, to that of solid gelatinous masses. *Chondrioderma* have the property of varying the consistence of the outer layer, and Pfeffer regards the tougher outer layer as a physiological product caused by reversible changes in cohesion. Pfeffer further states that not until the outer layer has been brought back to its original

<sup>4</sup> Macallum: *Jour. Biol. Chem.*, 1913, xiv, Proc. Amer. Soc. Biol. Chem., p. xxii.

<sup>5</sup> Jensen: *Anatomische Hefte*, 1905, xxvii, p. 842.

<sup>6</sup> Pfeffer: *Pflanzenphysiologie*, 1904, ii, p. 716.



fluid condition can changes in surface tension be regarded as factors in the ameboid movement.

Jensen obtained the figure of 6000 dynes per centimeter by dividing the weight sustained, by the circumference of the plasmodium thread. It would have been just as logical to divide the weight sustained by a steel wire, by its circumference and call the quotient the surface tension of the interface steel-air.

Countless measurements of the surface tensions of aqueous solutions (against air) have shown that the surface tension of water (about 70 dynes per cm.) cannot be raised very high. Some inorganic salt solutions have surface tensions against air as high as 85 dynes per cm.<sup>7</sup> On the other hand the surface tension between two solutions such as isobutyric acid in water and water in isobutyric acid is either nil or very nearly so.<sup>8</sup> Jensen's figure falls far outside the figures recorded for aqueous, or for any other type of, solution, that the writer has seen.

Consequently, Macallum's use of Jensen's figure and of data based upon it, in his theory of muscle contraction based upon changes in surface tension in the working muscle, may lead to erroneous results.

**The elimination of zinc.** WILLIAM SALANT and J. B. RIEGER. (*Pharmacological Laboratory, Bureau of Chemistry, U. S. Dep't of Agriculture, Washington, D. C.*) The experiments were made on rabbits. Zinc malate was given intravenously and zinc acetate subcutaneously. The urine collected for periods of 24-48 hours showed the presence of 1-2 mg. of zinc. Much larger amounts were found in the feces and contents of the posterior intestinal canal, after the subcutaneous injections. The quantities of zinc varied between 8.5 and 17.1 mg. in 24-48 hours, which represented 10-34 percent of the amounts introduced. The amounts of zinc eliminated by this channel were greater after intravenous injection, being 17-20 mg., or 40 percent of the quantity administered.

**The absorption and fate of tin in the body.** WILLIAM SALANT and L. P. TREUTHARDT. (*Pharmacological Laboratory,*

<sup>7</sup> Berg: *BIOCHEMICAL BULLETIN*, 1912, ii, p. 101.

<sup>8</sup> Whatmough: *Ztschr. f. physikal. Chem.*, 1901, xxxix, p. 184; Antonow: *Jour. de chimie physique*, 1907, v, p. 370.



*Bureau of Chemistry, U. S. Dep't of Agriculture, Washington, D. C.*) Tin, in the form of a double salt, was given subcutaneously and by mouth to different animals. Analyses of the urine and feces, and of the contents of the stomach and intestines, which were made gravimetrically and volumetrically, gave the following results: After the subcutaneous administration 5-15 percent was eliminated in the urine in 24-48 hours. The feces of the corresponding period contained much smaller amounts. The contents of the stomach and intestines, and the feces, contained as much or more tin than the urine. In some animals the amount of tin eliminated by the kidneys was smaller than that recovered from the gastro-intestinal contents and feces.

Analysis of the skin indicated the presence of 20-25 percent of the amount of tin injected.

When double salts of tin were given by mouth, small quantities of it were found in the tissues and in the urine, indicating that absorption from the gastro-intestinal canal takes place to a very small extent only, and may be insignificant in some animals.

The amount of tin found in the liver of rabbits at the end of 48 hours varied between 0.6 and 10.8 percent. The kidneys of such animals contained quantities varying between 1.6 and 8.2 percent of the amount of tin injected. Experiments on the absorption of the salt from the blood indicate that 85-95 percent may disappear in 2-3 hours after intravenous injection of 70-200 mg. of tin.

**The fate of creatine and creatinine when administered to rabbits.**<sup>9</sup> V. C. MYERS and M. S. FINE. (*Laboratory of Pathological Chemistry, New York Post-Graduate Medical School and Hospital.*) When creatine is administered subcutaneously to rabbits, in amounts varying between 50 and 100 mg. per kg. of body weight per day, 25-80 percent, depending upon the amount given, reappears in the urine unchanged, 2-10 percent is eliminated as creatinine, and about 15 percent is retained by the muscle. If introduced in small amounts, as much as 50 percent may be metabolised. We are inclined to attach considerable significance to the slightly increased excretion of creatinine as indicating the metabolic relationship between these two substances. The creatine content of the

<sup>9</sup> Myers and Fine: *Jour. Biol. Chem.*, 1913, xvi, p. 169.

muscle was raised from the normal of 0.52 percent to 0.55 percent (5 exp'ts) after the administration of creatine and to 0.56 percent (3 exp'ts) after the administration of creatinine.

**Comparison of the observed and computed heat production of cattle.**<sup>9a</sup> H. P. ARMSBY. (*The Institute of Animal Nutrition of The Pennsylvania State College.*)

**The role of oxidases in the curly-dwarf disease of potatoes.** H. H. BUNZEL. (*Laboratory of Plant Physiology, Bureau of Plant Industry, U. S. Dep't of Agriculture, Washington, D. C.*)

**A method for the estimation of total fat in infants' stools.** W. S. HUBBARD and D. M. COWIE. (*Pharmacy and Pediatric Departments, University of Michigan.*)

**The estimation of raffinose by a modified biological method.** C. S. HUDSON and T. S. HARDING. (*Division of Carbohydrate Investigations, Bureau of Chemistry, U. S. Dep't of Agriculture, Washington, D. C.*)

**The occurrence of a toxin in the bread mould, *Rhizopus nigricans*.**<sup>10</sup> R. A. GORTNER and A. F. BLAKESLEE. (*The Carnegie Institution of Washington.*)

**Studies in the comparative physiology of purine metabolism.** ANDREW HUNTER, M. H. GIVENS, and C. M. GUION. (*Department of Physiology and Biochemistry, Cornell University Medical College, Ithaca, N. Y.*)

**The calcium content of tuberculous areas in lung tissue.** MAX KAHN. (*Biochemical Laboratory, Columbia University.*)<sup>11</sup>

**Metabolism studies of five cases of endarteritis obliterans.** MAX KAHN. (*Chemical Laboratory, Beth Israel Hospital, New York.*)<sup>12</sup>

**A differential stain for mucins and mucoids.** LOUIS BERMAN and WM. J. GIES. (*Biochemical Laboratory, Columbia University.*)<sup>13</sup>

**A study of the influence of external hemorrhage on the parti-**

<sup>9a</sup> Armsby: *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 1794.

<sup>10</sup> Blakeslee and Gortner: *BIOCHEMICAL BULLETIN*, 1913, ii, p. 542.

<sup>11</sup> Kahn: *Ibid.*, 1913, ii, p. 458.

<sup>12</sup> Kahn: *Ibid.*, 1913, ii, p. 544.

<sup>13</sup> Berman and Gies: *Ibid.*, 1913, ii, p. 547.

tion of urinary nitrogen. OLIVE G. PATTERSON. (*Biochemical Laboratory, Columbia University.*)<sup>14</sup>

Further studies of edema. TULA L. HARKEY. (*Biochemical Laboratory, Columbia University.*)<sup>15</sup>

Biochemical studies of selenium. VICTOR E. LEVINE. (*Biochemical Laboratory, Columbia University.*)<sup>16</sup>

Pigments produced from thymol by ammonium hydroxid. BENJAMIN HOROWITZ and WM. J. GIES. (*Biochemical Laboratory, Columbia University.*)<sup>17</sup>

Metabolism studies of two cases of amaurotic idiocy. MAX KAHN and A. HYMANSON. (*Chemical Laboratory, Beth Israel Hospital, New York.*)<sup>18</sup>

Further studies of the permeability of lipin-collodion membranes. SAMUEL GITLOW and WM. J. GIES. (*Biochemical Laboratory, Columbia University.*)<sup>19</sup>

The origin and significance of salivary sulfocyanate. MAX KAHN and WM. J. GIES. (*Biochemical Laboratory, Columbia University.*)

Biochemical studies of dental caries. ALFRED P. LOTHROP and WM. J. GIES. (*Biochemical Laboratory, Columbia University.*)

I. K. PHELPS, *Secretary*

*Bureau of Chemistry,  
U. S. Department of Agriculture,  
Washington, D. C.*

<sup>14</sup> Patterson: *BIOCHEMICAL BULLETIN*, 1913, ii, p. 555.

<sup>15</sup> Harkey: *Ibid.*, 1913, ii, p. 550.

<sup>16</sup> Levine: *Ibid.*, 1913, ii, p. 552.

<sup>17</sup> Gies: *Ibid.*, 1912, ii, pp. 171 and 293; Horowitz: *Ibid.*, 1913, ii, p. 293.

<sup>18</sup> Hymanson: *Ibid.*, 1913, ii, p. 457.

<sup>19</sup> Elder: *Ibid.*, 1913, ii, p. 549; Gitlow, *Ibid.*

## THE BIOCHEMICAL SOCIETY, ENGLAND

### SCIENTIFIC PROCEEDINGS

INSTITUTE OF PHYSIOLOGY, UNIVERSITY COLLEGE, LONDON,  
*W. C., June 11, 1913, at 8.30 p. m.*—*C. G. L. Wolf*: A note on the estimation of lactic acid.—*S. Walpole*: Gas electrode for general use.—*J. A. Gardner and Miss C. M. Leetham*: On the respiration of fresh water fish.—*J. A. Gardner and Mr. Lander*: On the cholesterol content of the tissues of cats under various dietetic conditions.—*K. Goadby*: The action of vapors, given off from paint, upon the growth of bacteria.

ROTHAMSTED EXPERIMENTAL STATION, HARPENDEN, HERTS.,  
*July 12, 1913.*—*W. A. Davis and A. J. Daish*: (1) The quantitative estimation of maltose in plant materials; (2) A study of the formation of carbohydrates in the mangold leaf.—*H. E. Annett*: The sugar of the Indian date palm.—*A. Appleyard*: Apparatus for studying the gaseous reactions in soils.—*W. Buddin*: Plants grown on sterilised and unsterilised sick soils.—*A. J. Prescott*: A rapid method for determining  $P_2O_5$  in plant ash, soil extracts, etc.—*H. B. Hutchinson*: Effect of lime on the biological relationships of the soil.—*H. B. Hutchinson and K. McLennan*: Cellulose decomposition and nitrogen fixation. The beginnings of an atlas of soil bacteria.

LABORATORY OF PATHOLOGY, ST. THOMAS'S HOSPITAL, S. E.,  
*October 10, 1913, at 8.30 p. m.*—*C. Funk*: The chemical composition of the different parts of the maize grain obtained during the process of milling with reference to the etiology of pellagra.—*C. Funk*: Apparatus for concentrating solutions of highly unstable substances.—*H. MacLean*: (1) A simple method for preparing pure lecithin; (2) The action of lecithin as an activator of cobra venom in haemolysis; (3) Some observations on (*a*) acetone soluble phosphatides, (*b*) the part played by phosphatides in fatty degeneration; (4) The separation of "lecithin" into two somewhat similar

bodies, but containing different bases.—*H. J. Page*: The pigments of the brown algae.—*A. C. H. Rothera*: On mammary secretion.

#### MEMBERS ELECTED

*June 11.*—E. W. H. Cruickshank, M.B.; A. T. Daish; H. von Euler; C. G. P. Laidlaw; J. B. Leathes, F.R.S.; V. Lefebure, B.Sc.; V. Steele; C. H. Warner; George Winfield.

*July 12.*—Alfred Barnes; Winifred Cullis, D.Sc.; George Graham; O. C. Gruner, M.D.; P. W. Latham; R. Stenhouse Williams, M.D.

*Oct. 10.*—G. von Anrep; U. N. Brahmachari; Mary Fraser, B.Sc.; Edward Horton; Constance Leetham, B.Sc.; A. B. Macallum, Jun., M.D.; C. Myers Ward, M.D.; H. S. Raper, D.Sc.; A. Stead; Harold Wager, F.R.S.



# THE AGRICULTURAL COLLEGES AND EXPERIMENT STATIONS IN THE UNITED STATES

## I. THE AGRICULTURAL EXPERIMENT STATIONS IN THE UNITED STATES

### ALABAMA—

College Station: *Auburn*; J. F. Duggar.<sup>1</sup>

Canebrake Station: *Uniontown*; L. H. Moore.<sup>1</sup>

Tuskegee Station: *Tuskegee*; G. W. Carver.<sup>1</sup>

ALASKA—*Sitka*: C. C. Georgeson.<sup>2</sup>

ARIZONA—*Tucson*: R. H. Forbes.<sup>1</sup>

ARKANSAS—*Fayetteville*: Martin Nelson.<sup>1</sup>

CALIFORNIA—*Berkeley*: T. F. Hunt.<sup>1</sup>

COLORADO—*Fort Collins*: C. P. Gillette.<sup>1</sup>

### CONNECTICUT—

State Station: *New Haven*;  
Storrs Station: } E. H. Jenkins.<sup>1</sup>  
Storrs;

DELAWARE—*Newark*: H. Hayward.<sup>1</sup>

FLORIDA—*Gainesville*: P. H. Rolfs.<sup>1</sup>

GEORGIA—*Experiment*: R. J. H. DeLoach.<sup>1</sup>

GUAM—*Island of Guam*: J. B. Thompson.<sup>2</sup>

### HAWAII—

Federal Station: *Honolulu*; E. V. Wilcox.<sup>2</sup>

Sugar Planters' Station: *Honolulu*; H. P. Agee.<sup>1</sup>

IDAHO—*Moscow*: W. L. Carlyle.<sup>1</sup>

ILLINOIS—*Urbana*: E. Davenport.<sup>1</sup>

INDIANA—*Lafayette*: A. Goss.<sup>1</sup>

IOWA—*Ames*: C. F. Curtiss.<sup>1</sup>

KANSAS—*Manhattan*: W. M. Jardine.<sup>1</sup>

KENTUCKY—*Lexington*: J. H. Kastle.<sup>1</sup>

### LOUISIANA—

State Station: *Baton Rouge*;  
Sugar Station: *Audubon Park, New Orleans*;  
North La. Station: } W. R. Dodson.<sup>1</sup>  
*Calhoun*;  
Rice Station: }  
*Crowley*;

MAINE—*Orono*: C. D. Woods.<sup>1</sup>

MARYLAND—*College Park*: H. J. Patterson.<sup>1</sup>

MASSACHUSETTS—*Amherst*: W. P. Brooks.<sup>1</sup>

MICHIGAN—*East Lansing*: R. S. Shaw.<sup>1</sup>

MINNESOTA—*University Farm, St. Paul*: A. F. Woods.<sup>1</sup>

MISSISSIPPI—*Agricultural College*: E. R. Lloyd.<sup>1</sup>

### MISSOURI—

College Station: *Columbia*; F. B. Mumford.<sup>1</sup>

Fruit Station: *Mountain Grove*; Paul Evans.<sup>1</sup>

MONTANA—*Bozeman*: F. B. Linfield.<sup>1</sup>

NEBRASKA—*Lincoln*: E. A. Burnett.<sup>1</sup>

NEVADA—*Reno*: S. B. Doten.<sup>1</sup>

NEW HAMPSHIRE—*Durham*: J. C. Kendall.<sup>1</sup>

NEW JERSEY—*New Brunswick*: J. G. Lipman.<sup>1</sup>

NEW MEXICO—*State College*: Fabian Garcia.<sup>1</sup>

<sup>1</sup> Director.

<sup>2</sup> Special agent in charge.

<sup>3</sup> Acting director.

## NEW YORK—

State Station: *Geneva*; W. H. Jordan.<sup>1</sup>

Cornell Station: *Ithaca*; W. A. Stocking, jr.<sup>3</sup>

## NORTH CAROLINA—

College Station: }  
*West Raleigh*; }  
 State Station: } B. W. Kilgore.<sup>1</sup>  
*Raleigh*; }

NORTH DAKOTA—*Agricultural College*: J. H. Worst.<sup>1</sup>

OHIO—*Wooster*: C. E. Thorne.<sup>1</sup>

OKLAHOMA—*Stillwater*: L. L. Lewis.<sup>3</sup>

OREGON—*Corvallis*: J. Withycombe.<sup>1</sup>

## PENNSYLVANIA—

*State College*: R. L. Watts.<sup>1</sup>

*State College*: Institute of Animal Nutrition, H. P. Armsby.<sup>1</sup>

## PORTO RICO—

Federal Station: *Mayaguez*; D. W. May.<sup>2</sup>

Sugar Producers' Station: *Rio Piedras*; J. T. Crawley.<sup>1</sup>

RHODE ISLAND—*Kingston*: B. L. Hartwell.<sup>1</sup>

SOUTH CAROLINA—*Clemson College*: J. N. Harper.<sup>1</sup>

SOUTH DAKOTA—*Brookings*: J. W. Wilson.<sup>1</sup>

TENNESSEE—*Knoxville*: H. A. Morgan.<sup>1</sup>

TEXAS—*College Station*: B. Youngblood.<sup>1</sup>

UTAH—*Logan*: E. D. Ball.<sup>1</sup>

VERMONT—*Burlington*: J. L. Hills.<sup>1</sup>

## VIRGINIA—

*Blacksburg*: S. W. Fletcher.<sup>1</sup>

*Norfolk*: Truck Station, T. C. Johnson.<sup>1</sup>

WASHINGTON—*Pullman*: Ira D. Car diff.<sup>1</sup>

WEST VIRGINIA—*Morgantown*: E. D. Sanderson.<sup>1</sup>

WISCONSIN—*Madison*: H. L. Russell.<sup>1</sup>

WYOMING—*Laramie*: H. G. Knight.<sup>1</sup>

## II. THE AGRICULTURAL COLLEGES IN THE UNITED STATES

ALABAMA—*Auburn*: Charles C. Thach.<sup>4</sup>  
*Normal*: W. S. Buchanan.<sup>4</sup>

*Tuskegee Institute*: Booker T. Washington.<sup>5</sup>

ARIZONA—*Tucson*: Arthur H. Wilde.<sup>4</sup>

ARKANSAS—*Fayetteville*: Martin Nelson.<sup>6</sup>

CALIFORNIA—*Berkeley*: T. F. Hunt.<sup>6</sup>

COLORADO—*Fort Collins*: Charles A. Lory.<sup>4</sup>

CONNECTICUT—*Storrs*: C. L. Beach.<sup>4</sup>

DELAWARE—*Newark*: Geo. A. Harter.<sup>4</sup>  
*Dover*: W. C. Jason.<sup>4</sup>

FLORIDA—*Gainesville*: J. J. Vernon.<sup>6</sup>

*Tallahassee*: Nathan B. Young.<sup>4</sup>

GEORGIA—*Athens*: Andrew M. Soule.<sup>4</sup>  
*Savannah*: R. R. Wright.<sup>4</sup>

HAWAII—*Honolulu*: J. S. Donaghho.<sup>7</sup>

IDAHO—*Moscow*: W. L. Carlyle.<sup>6</sup>

ILLINOIS—*Urbana*: E. Davenport.<sup>6</sup>

INDIANA—*La Fayette*: J. H. Skinner.<sup>6</sup>

IOWA—*Ames*: R. A. Pearson.<sup>4</sup>

KANSAS—*Manhattan*: H. J. Waters.<sup>4</sup>

KENTUCKY—*Lexington*: J. H. Kastle.<sup>6</sup>  
*Frankfort*: G. P. Russell.<sup>4</sup>

LOUISIANA—*Baton Rouge*: Thos. D. Boyd.<sup>4</sup>

*New Orleans*: J. S. Clark.<sup>4</sup>

MAINE—*Orono*: R. J. Aley.<sup>4</sup>

MARYLAND—*College Park*: H. J. Patterson.<sup>4</sup>

*Princess Anne*: T. H. Kiah.<sup>5</sup>

MASSACHUSETTS—*Amherst*: Kenyon L. Butterfield.<sup>4</sup>

MICHIGAN—*East Lansing*: J. L. Snyder.<sup>4</sup>

MINNESOTA—*University Farm*, St. Paul: A. F. Woods.<sup>6</sup>

MISSISSIPPI—*Agricultural College*: G. R. Hightower.<sup>4</sup>

<sup>1</sup> Director.

<sup>2</sup> Special agent in charge.

<sup>3</sup> Acting director.

<sup>4</sup> President. <sup>5</sup> Principal. <sup>6</sup> Dean. <sup>7</sup> Acting president. <sup>8</sup> Acting dean.

- Alcorn*: J. A. Martin.<sup>4</sup>  
MISSOURI—*Columbia*: F. B. Mumford.<sup>6</sup>  
*Jefferson City*: B. F. Allen.<sup>4</sup>  
MONTANA—*Bozeman*: Jas. M. Hamilton.<sup>4</sup>  
NEBRASKA—*Lincoln*: E. A. Burnett.<sup>6</sup>  
NEVADA—*Reno*: Joseph E. Stubbs.<sup>4</sup>  
NEW HAMPSHIRE—*Durham*: Edw. T. Fairchild.<sup>4</sup>  
NEW JERSEY—*New Brunswick*: W. H. S. Demarest.<sup>4</sup>  
NEW MEXICO—*State College*: G. E. Ladd.<sup>4</sup>  
NEW YORK—*Ithaca*: W. A. Stocking, jr.<sup>8</sup>  
NORTH CAROLINA—*West Raleigh*: D. H. Hill.<sup>4</sup>  
*Greensboro*: James B. Dudley.<sup>4</sup>  
NORTH DAKOTA—*Agricultural College*: J. H. Worst.<sup>4</sup>  
OHIO—*Columbus*: H. C. Price.<sup>6</sup>  
OKLAHOMA—*Stillwater*: J. H. Connell.<sup>4</sup>  
*Langston*: Inman E. Page.<sup>4</sup>  
OREGON—*Corvallis*: W. J. Kerr.<sup>4</sup>
- PENNSYLVANIA—*State College*: Edwin E. Sparks.<sup>4</sup>  
PORTO RICO—*Mayaguez*: F. L. Stevens.<sup>6</sup>  
RHODE ISLAND—*Kingston*: Howard Edwards.<sup>4</sup>  
SOUTH CAROLINA—*Clemson College*: W. M. Riggs.<sup>4</sup>  
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## BIOCHEMICAL BIBLIOGRAPHY AND INDEX

### 4. Third quarter, 1913 (July–September)<sup>1</sup>

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**INDEX (SUBJECTS).** The numerals in the index (page 109) correspond with the numbered items in the bibliography. *Pages are not indicated*. Numerals held in groups by hyphens are plain abbreviations in accord with the indications of the first numeral of each such series (see footnote, p. 109). Abbreviations of words in the index are similar to those in the bibliography. Each *group of index references* is terminated by a semicolon; commas mark off *subdivisions of a general index subject*. *Names of authors are not indexed*.

**JOURNALS INCLUDED:** *Biochemische Zeitschrift (B.Z.)*, *Zeitschrift für physiologische Chemie (Z.p.C.)*, *Journal of Biological Chemistry (J.B.C.)*, *Biochemical Journal (B.J.)*, *Biochemical Bulletin (B.B.)*.

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<sup>1</sup> The preceding portions of this bibliography and index were published at pages 298, 470 and 559 of volume II of the *BIOCHEM. BULL.* (1913).

*Centralblätter* and year books, this running bibliography directs the reader to most of the main tracks through current literature on the leading biochemical subjects.

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<sup>2</sup> This series of abbreviations, illustrating all others in the index, represents the following sequence of numerals: 230, 250, 271, 275, 409. The numerals in bold-face type here are omitted from the abbreviations above.

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# BIOCHEMICAL NEWS, NOTES AND COMMENT

## EDITORIAL SUB-COMMITTEE:

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## I. GENERAL

**Necrology.** *John G. Curtis*, emer. prof. of physiology, Columbia Univ.—*J. Lucas-Championnière*, who introduced antiseptics into France.—*Jules Ogier*, formerly president of the Société de chimie, a member of the Comité consultatif d'hygiène publique de France, author of *Traité de chimie toxicologique*.—*Friedrich Seiler*, prof. of pharmaceutical chemistry, Lausanne.—*Charles Tellier*, the inventor of the cold storage system.—*William T. Wenzell*, emer. prof. of chemistry, Univ. of Cal., Col. of Pharmacy.

**Honors.** HONORARY DEGREES. Dr. *Svante Arrhenius* (Nobel Institute, Stockholm) and *Madam Curie* (Sorbonne, Paris) were among the foreign representatives at the recent meeting of the British Assoc. for the Adv. of Science upon whom the Univ. of Birmingham conferred its doctorate of laws. (See p. 117).

PRESIDENCY OF THE BRITISH ASSOC. FOR THE ADV. OF SCIENCE. Prof. *William Bateson*, director of the John Innes Horticultural Institute, has been elected president of the British Assoc. for the Adv. of Science for the meeting to be held next year in Australia.

OVATION. Prof. *J. L. Prevost* of Geneva was given an ovation recently on the occasion of his reaching the time limit of age and giving up the chair of physiology which he has so long filled. Delegates from medical societies and universities were present from



France, Italy and other countries, and several decorations and degrees were conferred on him. He was one of the founders of the *Revue Méd. de la Suisse Romande*, now in its thirty-third year, and has been a member of the editorial staff from the beginning.

LEGION OF HONOR. Dr. *Roux*, director of the Pasteur Inst., has been made a grand officer of the Legion of Honor.

AWARDS OF PRIZES. The Académie des sciences has awarded a *Montyon prize* (\$500) to Dr. *L. Ambard* for his memoir on the Renal secretion.—The *Raymond Horton-Smith prize* at the Univ. of Cambridge for 1913 has been awarded to *F. A. Roper* and *F. S. Scales*, who are adjudged equal for theses for the degree of M.D. Their subjects were: Creatinin and creatin metabolism, especially in reference to diabetes, and The electrocardiogram in diabetes.—The *Warren triennial prize* for 1913, amounting to \$500, has been awarded to Dr. Prof. *Arrigo Visentini*, instr. in pathol. anatomy in the Royal Univ. of Pavia, for his essay on the Function of the pancreas and its relation to the pathogenesis of diabetes.—The Intern. Med. Congr., at its London meeting, awarded its three prizes as follows: The *Moscow prize* to Prof. *Charles Richet* (Paris), for his work on anaphylaxis; the *Paris prize* to Prof. *A. von Wassermann* (Kaiser Wilhelm Inst. for Exp. Therapy), for his work on exp. therapy and immunity; and the *Hungary prize* to Sir *Almroth Wright* (London), for his work on anaphylaxis.

AWARD OF MEDAL. The *Baly medal* has been awarded, by the Royal Col. of Physicians, to Dr. *J. S. Haldane*, F.R.S., reader in physiology at the Univ. of Oxford.

Resignations, declinations and appointments.<sup>1</sup> DECLINATIONS. Professor *His*, who was asked to accept the appointment of director of the med. clinic as successor of von Noorden, at Vienna, has declined the honor.—Dr. *Franz Knoop*, assoc. prof. of physiol. chemistry, at Freiburg, has declined appointment to membership in the Rockefeller Inst.

APPOINTMENTS. Ala. Polytech. Inst. and Exp. Station: Dr. *L. S. Blake*, head of the dep't of pharmacy, vice Prof. *E. R. Miller* resigned.

<sup>1</sup> In this summary institutions from which *resignations* occurred are named in parenthesis. See page 129.

Bryn Mawr College: Dr. *A. R. Moore* (Univ. of Cal.), prof. of physiology.

Carnegie Institution, Nutrition Lab. (Boston): Dr. *Carl Tigerstedt* (Physiol. Inst., Univ. of Helsingfors), research associate.

Clark Univ.: Prof. *R. S. Lillic* (Univ. of Penn.), head of the biolog. dep't.

Cornell Univ. Med. Sch.: Dr. *Joseph C. Bock* (Carnegie Nutrit. Lab., Boston), instr. in chemistry.

Inst. for Infec. Diseases (Berlin): Prof. *Friedrich Loeffler* (Greifswald), director, succeeding Prof. Gaffky.

Iowa Agric. Exp. Sta. (Ames): Dr. *P. L. Blumenthal*, assis. chemist, to conduct investigations on the chemistry of orchard insecticides and fungicides.

Jefferson Med. Col.: Messrs. *C. A. Smith* (Penn. State Col.), demonstrator and *Marvell Sillman*, instr., in physiol. chemistry.

Kaiser Wilhelm Inst. for Exp. Therapeutics (Berlin): Prof. *A. von Wassermann*, director; Prof. *Carl Neuberg*, demonstr. in the chemical division.

Kaiser Wilhelm Society, Research Inst. for Biology: Dr. *Carl Correns* (prof. of botany, Münster), director; Dr. *Hans Spemann* (prof. of zoology, Rostock), assis. director; Dr. *Warburg*, in charge of the work in cell physiology.

Mass. Inst. Tech.: Mr. *R. S. Weston*, assis. prof., dep't of biology and public health.

Peter Bent Brigham Hosp. (Boston): Dr. *Francis H. McCrudden* (Rockefeller Inst.), director of the laboratories.

St. Louis Univ. Sch. of Med.: Dr. *Don R. Joseph* (Bryn Mawr), prof. of physiology.

U. S. Dep't of Agric., Bur. of Chem.: Dr. *Isaac K. Phelps* (Bur. of Mines, Pittsburgh), chemist; chief of the division of organic chemistry investigations.

U. S. Public Health Service, Hygienic Lab. (Wash.): Dr. *Carl Voegtlin* (Johns Hopkins Univ.), prof. of pharmacology; Dr. *E. B. Phelps* (Mass. Inst. of Tech.), prof. of chemistry.

Univ. of Ala. Med. Sch.; Dr. *Andrew H. Ryan* (instr. in physiology and pharmacology, Univ. of Pittsburgh), prof. of physiology, in succession to Dr. J. Van de Erve, resigned, now prof. of physiology, Marquette Univ.

Univ. of Bonn: Dr. *H. Selter*, acting director of the Hygienic Inst., succeeding Prof. Kruse.

Univ. of Cal.: Dr. *Fritz W. Woll* (Univ. of Wis.), prof. of animal

nutrition; Scripps Inst. of Biolog. Research: Dr. *F. B. Sumner*, biologist.

Univ. of Ill. Med. Sch. (Chicago): Dr. *Geo. P. Dreyer*, prof. of physiology; Mr. *J. Craig Small*, assis. in physiol. chemistry; Dr. *Bernard Fantus*, prof. of pharmacology; Dr. *Edgar D. Coolidge*, prof. of materia medica and therapeutics. (See *BIOCH. BULL.*, 1913, ii, pp. 575 and 578.)

Univ. of Leeds: Dr. *Charles Crowther*, prof. of agric. chemistry, in charge of the work in animal nutrition; Dr. *H. W. Dudley* (Herter Laboratory), lecturer in biochemistry.

Univ. of Leipzig: Dr. *Walter Kruse* (Bonn), prof. of hygiene and director of the Hygienic Inst., as successor to Prof. Hofmann.

Univ. of Neb. Med. Sch. (Omaha): Dr. *Irving S. Cutter*, prof. of biolog. chemistry; Dr. *A. E. Gunther*, prof. of pharmacology.

Univ. of Penn.: Dr. *Howard B. Lewis* (Sheff. Sci. Sch., Yale), instr. in physiol. chemistry (Sch. of Med.); Dr. *Hermann Prinz*, prof. of materia medica and therapeutics (Sch. of Dentistry).

Univ. of Pittsburgh: Mr. *Orville J. Walker*, assis. in physiology and pharmacology.

Univ. of Vienna: Prof. *Julius Mauthner*, director of the Medico-chemical Inst., vice Prof. E. Ludwig retired; Prof. *Hugo Salomon*, director of the med. clinic, vice Dr. Carl von Noorden resigned.

Univ. of Wis.: Dr. *Stephen M. Babcock*, prof. emeritus of agric. chemistry; Dr. *E. R. Miller* (Ala. Polytech. Inst.) acting assis. prof. of plant chemistry.

Western Reserve Univ.: Dr. *Roy G. Pearce*, instr. in physiology (promotion).

**Alvarenga prize.** The Col. of Physicians, Phila., announces that the next award of the *Alvarenga prize*, being the income for one year of the bequest of the late Señor Alvarenga and amounting to about \$180, will be made on July 14, 1914, provided that an essay worthy of the prize shall have been offered. Essays intended for competition may be on any subject in medicine, but cannot have been published. They must be typewritten, and if written in a language other than English, should be accompanied by an English translation, and must be received by the secretary of the college on or before May 1, 1914. Each essay must be sent without signature, but must be plainly marked with a motto and be accompanied by a sealed envelope having on its outside the motto of the paper and within the name and address of the author. It is a condition of the competition that the

successful essay or a copy of it shall remain in possession of the college; other essays will be returned on application within three months after the award. Further information may be obtained on application to Thomas R. Neilson, M.D., sec'y, 19 S. 22d St., Philadelphia.

**Grants.** At the recent meeting of the British Assoc. for the Adv. of Science, at Birmingham, grants in aid of scientific research amounting to about \$6,000 were made. The grants of special interest to biochemists are the following: CHEMISTRY—Dr. *W. H. Perkin*, study of hydroaromatic substances, £15; Prof. *H. E. Armstrong*, dynamic isomerism, £25; Prof. *F. S. Kipping*, transformation of aromatic nitroamins, £15; *A. D. Hall*, plant enzymes, £25; Prof. *W. J. Pope*, correlation of the crystalline form with molecular structure, £25; Prof. *H. E. Armstrong*, solubility phenomena, £15.—PHYSIOLOGY: Prof. *E. A. Schäfer*, the ductless glands, £35; Prof. *A. D. Waller*, anesthetics, £20; Prof. *J. S. Macdonald*, calorimetric observations, £40; Prof. *C. S. Sherrington*, mammalian heart, £30.

The Commit. of the Paris Acad. of Sciences, appointed to consider the distribution of the Bonaparte research fund, has made the following recommendations, among others, for 1913: *R. Coquidé*, 2,000 francs, to assist him in his study of the turf lands of the north of France from the agricultural point of view; *Paul Becquerel*, 2,000 francs, for the continuation of his researches on the influence of radioactive substances on the nutrition, reproduction, and variation of some plant species; *M. Lormand*, 2,000 francs, for the purchase of a sufficient quantity of radium bromid for methodical researches on the influence of radioactivity on the development of plants.

**Endowment funds.** FOREIGN. *Ernest Solvay*, the discoverer of a process for the manufacture of soda, celebrated the fiftieth anniversary of that discovery on Sept. 2 at Brussels by giving more than \$1,000,000 to educational and charitable institutions and the employees of his firm. The Universities of Paris and Nancy each received \$100,000.—Dr. *Gavin P. Tennent*, of Glasgow, has bequeathed £25,000 to the Univ. of Glasgow, to be applied for such



objects in connection with medicine as the trustees may determine. The Univ. has also received a legacy of £5,000 by the late Mr. *William Weir*, ironmaster, the income of which is to pay for an additional assist. to the prof. of materia medica.

AMERICAN. *Mrs. Russell Sage* has given \$34,000 to Syracuse Univ., of which \$30,000 is for the Joseph Slocum Agric. Col.—The General Educ. Board has announced a gift of \$1,500,000 to the med. sch. of Johns Hopkins Univ., to be known as the *William H. Welch Endowment for Education and Clinical Research*, in recognition of Dr. Welch's distinguished service to the cause of medical education in America. This is the greatest gift ever made by the board to a single institution of learning. The proposed plan of spending the money opens the way for a new era in med. science. Briefly it is this: To so reorganize the med. sch. as to pay out of the income from the gift such salaries to the men who occupy the chairs of medicine, surgery and pediatrics (and to their assistants) as will enable them wholly to drop their private practices and devote their entire time, ability and lives to the advancement of their particular branches. The departments which it affects are at present presided over by Dr. Lewellys F. Barker, prof. of medicine; Dr. W. S. Halsted, prof. of surgery; Dr. John Howland, prof. of pediatrics.

**Notes on radium.** APPRECIATION OF MADAME CURIE. All the world knows how Madame Curie (coming from Warsaw as Marie Skłodowska to work in Paris), inspired by the spontaneous radioactivity newly discovered by Becquerel, began in 1896 a metrical examination of the radioactivity of minerals of all kinds; and how, when a uranium residue showed a value larger than could have been expected from its uranium content, she, with exemplary skill and perseverance, worked down some tons of this material (given her by the Austrian government on the instigation of Prof. Suess), chemically dividing it and retaining always the more radioactive portion, until she obtained evidence first of a new element which she christened polonium, in memory of her own country, and then after months of labor succeeded in isolating a few grains of the other and more permanent substance now so famous—a substance which not only exhibits physical energy in a new form, but is



likely to be of service to suffering humanity. Of the metallic base of this substance she determined the atomic weight, finding a place for it in Mendeléeff's series; and with the aid of her husband, whose lamentable death was so great a blow to science, she proceeded to discover many of its singular properties, some of them so extraordinary as to rivet the attention of the world. Subsequent workers engaged in the determination of numbers belonging to either of her special elements, radium and polonium, have sought her advice, and it has proved of the utmost value. (Sir OLIVER LODGE, president of the British Assoc. for the Adv. of Science and principal of the Univ. of Birmingham, in introducing Madam Curie to the Univ. for the honorary degree of LL.D.: *Science*, 1913, xxxviii, p. 521.)

NATIONAL RADIUM INSTITUTE. The Director of the Bureau of Mines authorizes the announcement that a cooperative agreement has been entered into with the newly organized National Radium Inst., whereby the Bureau obtains the opportunity of a scientific and technological study of the mining and concentrating of carnotite ores and of the most efficient methods of obtaining radium, vanadium and uranium therefrom, with a view to increased efficiency of production and the prevention of waste. The institute was recently incorporated with the following officers: President, *Howard A. Kelly*, vice-president, *Curtis F. Burnam*, secretary and treasurer, *Archibald Douglas*, additional directors, *James Douglas* and *E. J. Maloney*.

The institute has no connection with the mining of pitchblende, details of which recently appeared in the Denver papers. It has, however, obtained the right to mine twenty-seven claims in the Paradox Valley region, among which are some of the best mines in this richest radium-bearing region of the world. Nearly one hundred tons of high-grade carnotite have already been procured. Under the agreement with the Bureau of Mines, the technical operations of the mines and mill are to be guided by the scientific staff of the Bureau. Work will begin in an experimental plant to be erected in Colorado, using entirely new methods developed at the Denver office of the Bureau of Mines. Concentration experiments also will be conducted in the Paradox, probably at the Long Park claims, and if successful will be applied to reducing the wastes that now

take place. Within a year at most, the mill operations should make results certain and the extraction of ore and production of radium will then be continued on a larger scale. The separation of uranium and vanadium will also be studied, a contract having already been signed for all of these by-products that may be obtained. All processes, details of apparatus and plant, and general information gained will be published for the benefit of the people.

The institute is supplied with sufficient funds to carry out its plans. It has been formed for the special purpose of procuring enough radium to conduct extensive experiments in radium therapy with special reference to the curing of cancer. It also expects to carry on investigations regarding the physical characteristics and chemical effects of radium rays and hopes in time to be able to assist or perhaps even duplicate the effects of these rays by physical means.

Actual experience, especially of the institute's president, in the application of the 650 mg. of radium and 100 mg. of mesothorium already in his possession, have led him and his associates to believe that with larger supplies many of the variables that can not now be controlled may be fully correlated, and that radium may become the most effective agent for the treatment of cancer and certain other malignant diseases. Important results have already been obtained by using high concentration of the gamma rays of radium with the alpha rays entirely cut off and the beta rays largely eliminated. Hospital facilities in both Baltimore and New York are already supplied. (CHARLES L. PARSONS: Address to the 16th Annual Conv. of the Amer. Mining Congr., Phila., Oct. 20-24: *Science*, 1913, xxxviii, p. 612.)

IMPORTANT DISCOVERIES AT THE RADIUM INST., LONDON. From the Radium Inst. some important discoveries in radium therapy are announced. At the Inst. it has been demonstrated that radium emanation has exactly the same properties as pure radium and is as efficient for curative purposes. This is a discovery of the highest practical importance, for previously radium treatment could be given only at the Inst., as it was not practicable to lend this extremely valuable and limited substance. Now the emanation fixed in a hollow plate or tube, is sent to physicians for use on patients. Thus, if a physician wants 200 mg. of radium for use on a patient,

its cost, \$20,000, would be prohibitive. But for a comparatively trifling sum the Inst. can supply a plate containing radium emanation which will have the same effect. There is this difference, however, the activity of the emanation decreases, falling to one-half strength in three and one-half days. At present, 1 gm. of radium is devoted wholly to producing emanation for distribution, and as the demand is so great, 1.5 gm. is about to be used. Another branch of the activity of the Inst. is the supply of water impregnated with radium emanation for consumption in certain affections. The Inst. is supplying radium-emanation solution of a strength of from 1 to 2 millicuries per liter.

The Radium Inst. was opened in Aug., 1911, and since that time the work has steadily increased. At first it was open from 8 a. m. to 6 p. m. for the purpose of treating patients. So numerous were the poor patients that a night clinic had to be added sixteen months ago. It is open until 11.30 p. m., and sometimes until midnight. . . . During the month of August the Inst. was closed in order that members of the staff, who were working at high pressure and all of whom have radium burns on their hands, might have a holiday and rest, which is the only known cure for these burns.

The quantity of radium in the Inst. is, at the present price, of the value of \$400,000, and amounts to 4 gm. (LONDON LETTER: *Jour. Amer. Med. Assoc.*, 1913, lxi, p. 1469.)

DANGERS OF RADIUM. The assist. med. sup't, Dr. Arthur Burrows, of the Radium Inst., London, states that most of the staff have been burned to a greater or less extent at some time or another. In his own case he found the skin peeling off his fingers when he went to play golf. The nurses, however, who do most of the actual handling, suffer most. In addition to the more or less painless skin-peeling, the finger nails become brittle and split down the center, ulcerated spots appear, and in time the hands become totally anesthetic. It is curious that the hands of those who have much to do with radium are always far more susceptible to heat than to cold. Gloves are not much protection. The only thing to do when the fingers show these symptoms is to have nothing to do with radium until they recover. Those who develop burns are usually given some work in connection with the Inst. which does not involve

immediate contact with the element. Radium in course of time burns most things with which it comes in contact. For instance, the lining of the boxes in which it is kept is often entirely eaten away. The ill effects are not felt in the human body until a fortnight after the contact. It eats away the abnormal tissues, such as carcinoma, sarcoma, etc., and leaves the surrounding normal tissues in an ordinary condition. In its antipathy to abnormal tissues lies its curative properties in these cases. But in time, or as the result of excessive application, radium will have an effect also on the normal tissues. A subsidiary effect on the patient is increased susceptibility to changes of temperature over areas that have been treated with radium. Many patients who have had rodent ulcers and superficial skin lesions, cured with radium, experience great discomfort at the site of the old lesion when very cold or very warm air plays on it. This susceptibility, however, gradually disappears in two or three months. A marked condition of lethargy is frequently, it might almost be said invariably, noted in patients receiving prolonged exposures with large quantities of heavily screened radium. It generally makes its appearance about the fourth day of the treatment, and passes off within a few days of the cessation of the exposures. (LONDON LETTER: *Jour. Amer. Med. Assoc.*, 1913, lxi, p. 1549.)

MUNICIPAL OWNERSHIP OF RADIUM. On favorable reports as to the therapeutic effects of mesothorium in cancer, the communal authorities of Essen have determined to purchase 200 mg. of the preparation. Half of the necessary sum, \$10,000, has been raised by private subscription and the rest has been appropriated by the communal authorities.—A bureau for the distribution of radium and mesothorium has been founded in the Hamburg Inst. for Cancer and Tuberculosis Research, which was founded a short time ago. The object is to secure as large a quantity of these preparations as possible in a short time and place them at the disposal of the public. At present about 150 mg. of radium bromid are on hand; this quantity is to be doubled in about two weeks and there is a prospect of securing further amounts. The preparations are to be loaned to physicians.—The favorable results which have been obtained with mesothorium radiations in carcinoma by the gynecologists Bumm,



Krönig and others have excited great attention<sup>1</sup> in our newspapers and partly under the pressure of public opinion and partly instigated by the wishes of the directors of the hospitals, the municipal authorities in a number of cities have determined to purchase some mesothorium and radium. Berlin has appropriated \$50,000 for this purpose, and \$200,000 have been appropriated for the same purpose by the Prussian Department of Education. It is to be hoped that further success will justify this not inconsiderable material sacrifice. —The great rush for the purchase of mesothorium and radium by municipalities, has been suddenly checked by the city of Munich. The city government of that city has refused for the present to carry out the resolution to buy \$50,000 worth of this costly material. It is believed that there are positive evidences that the factories engaged in producing mesothorium are raising the price unduly. For this reason, more exact information is to be obtained by the municipal authorities before the purchase of the preparation is consummated in Munich and other cities. (BERLIN LETTER: *Jour. Amer. Med. Assoc.*, 1913, lxi, pp. 613, 1055, 1308 and 1470.)

The Prussian Government has purchased a gram of radium at the cost of \$87,500 for hospital and scientific use.

The Prussian ministry of education, which a short time ago made grants of money to the univ. clinics at Berlin, Halle and Kiel, enabling them to procure radium or mesothorium for the treatment of cancer, is now said to have placed \$200,000 in the estimates of next year for further purchases.

There was a section of radiology at the last Intern. Congr. of Med., for the first time in the history of the congress.

**Meetings of societies and congresses.** BRITISH ASSOC. FOR THE ADV. OF SCIENCE. The annual meeting of the British Assoc. for the Adv. of Science was held in Birmingham. The attendance numbered 2,500.

*Hormones.* In the Sect. of Physiology the most important paper was that on internal secretions, by Prof. Schäfer. He pointed out that the convenient term hormone, introduced by Starling (from ὁρμάω, I excite) while applicable to the active principle of many internal secretions, has been extended to all and is wrongly



applied to principles which do not excite, but check activity. For these he suggested the term chalone (from χαλδω, I relax). It is, however, desirable to have a term which includes both the hormones and chalones. The one quality which distinguishes them is their drug-like effect on the organs and tissues. A convenient term, suggested by Prof. W. R. Wardie, is *autacoid* substance.

*Discussion of the origin of life.* A large audience attended a combined meeting of the sections of physiology, zoology and botany for a discussion on the origin of life. At this meeting the subject was introduced by Dr. B. Moore, prof. of biochemistry in the Univ. of Liverpool. He regarded the problem as an experimental one and said that he could demonstrate a step which connected inorganic with organic matter. The world of living plants and animals depends on the synthesis of organic from inorganic compounds by the chlorophyl of plants acting as a transformer of light energy into chemical energy. This state of affairs must have evolved from something more simple, for chlorophyl is one of the most complex of known organic substances. In considering the origin of life the start must be made in a purely inorganic world. As the results of eighteen months' experimental work, he believed that he has obtained evidence of the first step in organic evolution. When dilute solutions of colloidal ferric hydroxid or the corresponding uranium compound are exposed to strong sunlight, there are synthesized the same compounds as are formed in the first stage of organic synthesis by the green plant—formaldehyd and formic acid. If now they considered a planet cooling down and exposed to sunlight, at first elements only would be present. As it cooled, binary compounds would form and then simple crystalloid salts. By the union of single molecules into groups of fifty or sixty, colloidal aggregates appeared. As these increased in complexibility they became more delicately balanced (labile). They were easily destroyed by sudden changes in environment, but within certain limits were peculiarly sensitive to energy changes and could take up energy in one form and transform it into another. These labile colloids took up water and carbon dioxid and, utilizing the sunlight streaming onto the plant, produced the simplest organic structures. Next these structures reacting with themselves and with nitrogenous inorganic mat-

ter, continued the process and built up more and more complex and also more labile organic colloids, until finally these acquired the property of transforming light energy into chemical energy.

In the discussion which followed, *Sir Oliver Lodge* agreed that new possibilities entered matter with the increase of size and complexity of the molecule. A molecule sufficiently complex and sufficiently unstable and supplied with energy by the sunlight apparently gave the chemical substratum for the operations of life. It was potential living matter. This has not been made yet, but he has not much doubt that it might be done. To produce potential living matter, however, is not to produce life. He regards life as of a higher order, for he does not consider the universe limited entirely to what we know.

*Professor Armstrong* said that as a chemist he is not for a moment prepared to accept Schäfer's contention that it is probable that we shall ever be able to produce life. This would mean a series of operations so infinitely complex that it is not within our power to pronounce any opinion on its possibility. The dominant word in Moore's paper was the word "colloid." It is a blessed word among the physiologists at the present day, but like so many blessed words is used for wrapping up ignorance.

*Professor Hartog* said that there was a tremendous amount of scientific "bluff" in the assertion that there was a consensus of opinion among biologists that life was only one form of chemical and physical action which could be produced in the laboratory. The greatest biologists held aloof from such dogmatism. (LONDON LETTER: *Jour. Amer. Med. Assoc.*, 1913, lxi, p. 1307.)

INTERN. MED. CONGR. The Intern. Med. Congr. (17) was formally opened at Albert Hall, London, Aug. 6, by Prince Arthur of Connaught.

*Ehrlich on chemotherapy.* At the general session on Friday, Aug. 8, Professor Ehrlich delivered, in German, the address in pathology taking for his theme: Chemotherapy. After referring to the work of Jenner, Lister, Sir Patrick Manson, Ross, Castellani, Bruce, Leishman and others on the protozoan diseases, he entered into a technical explanation of the principle of chemotherapy, especially with reference to the work done in elaborating salvarsan. He ex-

plained that salvarsan has not only a direct parasitocidal action, but that immunity of parasites to such action could be accounted for only by a purely chemical diminution of their affinity; and a complete exhaustive knowledge of the various chemical peculiarities of a parasite, which he called the "therapeutic physiology of the parasitic cell," is essential for its successful chemotherapeutic treatment. Certain chemical peculiarities are found in many different kinds of parasites. In proportion as more of these chemical affinities are discovered, the greater is the possibility of successful chemotherapy. He still keeps in view the idea of freeing the body of micro-organisms by one or at most two injections of the proposed remedy, and in his animal experiments this principle is still being pursued. He looks forward to the extension of the principle of chemotherapy as a means of bridging the gaps which still exist in our knowledge of the treatment of some diseases. In the diseases involving protozoa and spirilla, good results have already been gained. In a series of other diseases, such as small-pox, scarlatina, typhus, and perhaps also yellow fever, but above all the infectious diseases caused by invisible germs, there is a bright prospect of success. In the common bacterial diseases due to streptococcus, staphylococcus, and the micro-organisms of typhoid, dysentery and tuberculosis, he feels that the struggle is a hard one, but that success in these diseases will also be attained on the principle of chemotherapy. (LONDON LETTER: *Jour. Amer. Med. Assoc.*, 1913, lxi, p. 610.)

*On the "art of conciseness."* The program was generally overcrowded and speakers often raced the clock to get in what they wanted to say in the allotted time, and were brought to a premature end by the chairman's bell. As in all medical gatherings, the incapacity of even those who were eminent and had something to say, to say it properly and concisely, was painfully evident. The fifteen minutes allotted to a speaker, if properly used, was in most cases amply sufficient for the presentation of his conclusions and his reasons for them, but want of conciseness of expression as well as want of judgment in suppressing unnecessary details prevented this. Instead of brief but sufficient general description, worse than useless details which only wearied the audience were presented. It is curious that no one seems to trouble about the reform of this uni-

versal evil. The man who could compel the education of medical authors in the *art of conciseness*, before they be permitted to speak or write, would deserve a place in history among the benefactors of humanity. (LONDON LETTER: *Jour. Amer. Med. Assoc.*, 1913, xli, p. 612.)

AMER. CHEM. SOC'Y. The annual meeting (48) of the Amer. Chem. Soc'y was held at Rochester, N. Y., Sept. 8 to 12. This was the first meeting in Sept. under the newly adopted constitution. The large number present and the enthusiasm of the meeting amply justify the change in date from the Christmas holidays to the fall of the year.

Dr. *Charles L. Parsons* was re-elected secretary of the society, and Dr. *A. P. Hallock*, treasurer, for a period of three years, under the revised constitution. Prof. *W. A. Noyes* was re-elected editor of the *Jour. of the Amer. Chem. Soc'y*, and the board of associate editors was continued, with the exception of Drs. *H. P. Talbot* and *A. A. Noyes*, who asked to be relieved of this duty. Prof. *W. Lash Miller*, of the Univ. of Toronto, was elected to the board with special reference to physical chemistry. Prof. *M. C. Whitaker* was re-elected editor of the *Jour. of Indus. and Eng. Chem.*, and the board of associate editors was continued and the editorial staff strengthened by the addition of two assist. editors. Prof. *A. M. Patterson* was re-elected editor of *Chemical Abstracts*, and Drs. *J. J. Miller* and *E. J. Crane* assoc. editors. (See page 76.)

INTERN. CONGR. OF REFRIGERATION. The Third Int. Cong. of Refrig., with an attendance of nearly 2,000 delegates, over 400 of whom were from abroad, convened in Washington and Chicago, from Sept. 15 to Oct. 1. The officers of the Third Section (on the "application of refrigeration to foods for the purpose of conserving and preserving them") were: President, Dr. *Harvey W. Wiley*; vice-pres., Mr. *C. H. Parsons*; sec'y, Dr. *M. E. Pennington*; additional member of the sect. commit., Prof. *R. M. Allen*, Prof. *H. J. Eustace*, Mr. *H. C. Gardner*, Prof. *Wm. J. Gies*, Mr. *J. L. Hughes*, Prof. *W. A. Stocking*, Prof. *A. V. Stubenrauch*, Mr. *R. H. Switzler*.

Miscellaneous items. LANE LECTURES. The fourteenth course of Lane med. lectures was delivered in Lane Hall, San Francisco,



on the evenings of Sept. 3, 4, 5, 8 and 9, by Prof. Sir E. A. Schäfer, prof. of physiology, Univ. of Edinburgh, on Internal secretion in general, The thyroparathyroid glands, The adrenal glandular apparatus, The pituitary body, The influence of internal on other secretions. Prof. Schäfer also delivered at Stanford University a lecture on Methods of resuscitation.

PASTEUR INST. TWENTY-FIVE YEARS OLD. Owing to the renown of Pasteur's studies of rabies, an international subscription, which was opened by the Acad. des Sciences de Paris, soon amounted to \$500,000 and permitted the foundation, twenty-five years ago (Nov. 18, 1888), of the Institut Pasteur. At present the Inst. is a center at once of scientific research, of higher instruction and of therapeutic treatment. It is divided into three principal sections: microbiologic, serotherapeutic, and biochemical. One of the sources of superiority of the Pasteur Inst. consists in its independence. It was founded and is carried on without official superintendence and hence has a spirit of initiative and of adaptiveness which administrative oversight scarcely permits to government establishments.

SCHOOL FOR PUBLIC HEALTH OFFICERS. Harvard Univ. and the Mass. Inst. of Tech. will cooperate in maintaining a Sch. for Public Health Officers. Prof. *M. J. Rosenau* (Harvard) is the director. The work of the school will be under his immediate supervision, in association with Profs. *W. T. Sedgwick* and *Geo. C. Whipple* as an administrative board.

APPRECIATION OF THE SERVICES OF THE COMMIS. ON ELECT. SHOCK. At the last annual meeting of the National Elect. Light Assoc., the following resolution was unanimously adopted:

*Whereas*, The Assoc. has accomplished a most creditable piece of humanitarian work in the issuance of its rules on resuscitation from electric shock used throughout the world and approved formally by other industries, the national government and state boards; *therefore*, be it

*Resolved*, That the thanks of this association be extended to the Med. Commis. for its splendid results, and also to the Amer. Med. Assoc., without whose active cooperation these laudable results could never have been achieved.

The work of this commis. is monumental and its effects will be



widespread. It is an excellent illustration of the valuable results which can be secured through practical cooperation between the medical profession and enlightened business men for the saving of life and the prevention of accidents. (EDITORIAL: *Jour. Amer. Med. Assoc.*, 1913, lxi, p. 1637.)

The commis. consists of Prof. *Walter B. Cannon*, chairman; nominated by the Amer. Med. Assoc., Prof. *Yandell Henderson*, Dr. *George W. Crile*, Dr. *S. J. Meltzer*, nominated by the Nat. Elec. Light Assoc., Prof. *Edward A. Spitzka*, Mr. *W. C. L. Elgin*, nominated by the Amer. Inst. of Elec. Engineers, Prof. *Elihu Thompson*, Dr. *Arthur E. Kennelly*, Mr. *W. D. Weaver*, sec'y (elected by the commis.).

ETHER DAY. The sixty-seventh anniversary of Ether Day was celebrated in the lower amphitheater of the outpatient's dep't of the Mass. Gen. Hosp., Oct. 16. The principal address was delivered by Dr. M. J. Rosenau.

CARBATES. In this age of method, accuracy and conciseness, we may say sulphates instead of sulphurates; phosphates for phosphorates (better still, sulfates and fosfates); nitrates for nitrogenates; chlorates for chlorinates. Why should we not say *carbates* instead of carbonates? We already say carbides instead of carbonides; why should we not follow the fashion consistently and say *carbates*? We should then have the word carbation to mean the formation of carbates, leaving the word carbonation to refer to the development of carbon in a substance which would fittingly correspond to the present word carbonize, and so avoid a puzzling ambiguity. Furthermore, the saving of time and printer's ink would amount to something in a word so often used. (J. E. TODD: *Science*, 1913, xxxviii, p. 270.)

MARK CRUCIBLES WITH INK. It is a more or less common practice to mark porcelain crucibles or other articles with ordinary fountain pen ink. The usual directions are to dry and subsequently heat in the blast, repeating the whole operation as often as necessary to obtain a clear brown figure. It is a saving of considerable time if a convenient area of the crucible first be heated in a Bunsen flame and the figure then drawn with a fountain pen. The ink

dries instantaneously, and in one operation leaves a coating of any thickness desired. Such figures are distinct even when exceedingly small, and have the advantage of being practically permanent. (ROSS ALLEN BAKER: *Chemist-Analyst*, 1913, Aug., p. 12.)

## II. COLUMBIA UNIVERSITY BIOCHEMICAL ASSOCIATION

### I. General notes

**Marriages:** On July 20, Miss Jessie Archibald Moore and Dr. Alfred Henri Rahe.—On Sept. 25, Dr. Martha Ornstein and Dr. J. Bronfen Brenner.

**Engagement:** Miss Eleanor Riehm, of Newark, N. J., and Dr. Clayton S. Smith.

**Appointments.**<sup>1</sup> Dr. *Chas. F. Bolduan*, lect. on hygiene and sanitation, N. Y. Univ. and Bellevue Hosp. Med. Col.—Dr. *Sidney Born* has been retained by Prof. M. C. Whitaker to conduct an extensive investigation of the composition and constituents of certain vegetable oils, with particular bearing on the organic substances occurring in extremely small proportions.—Dr. *E. D. Clark* (instr. in chemistry, Cornell Univ. Med. Sch.), soil biochemist, Bur. of Chemistry, U. S. Dep't of Agric.—Dr. *C. B. Coulter*, assis. in pathology, Columbia Univ.—Mr. *Fred D. Fromme*, assis. in botany, Indiana Exp. Station.—Dr. *T. Stuart Hart*, assis. prof. of clin. medicine, Columbia Univ. (promotion).—Dr. *Homer D. House* (assoc. director and lect. on botany and dendrology, Biltmore Forest Sch.), assis. state botanist of New York.—Dr. *Emile F. Krapf*, research chemist and chief of the pharmaceut. dep't, Radium Research Lab. of the Standard Chem. Co., Pittsburgh.—Dr. *Max Morse* (prof. of biology, Trinity Col.), instr. in biochemistry, Univ. of Wis.—Dr. *Reuben Ottenberg*, instr. in bacteriology, Columbia Univ.—Mr. *P. W. Punnett*, assis. in chemistry, Columbia Univ.—Dr. *Jacob Rosenbloom* (assis. prof. of biochemistry, Univ. of Pittsburgh), biolog. chemist, Western Penn. Hospital, Pittsburgh.—Dr. *Charles Hendee Smith*, instr. in diseases of children, Columbia Univ.

<sup>1</sup> See footnote, page 113.

**Investigators at Woods Hole.** The following members of the Assoc. were among the investigators, during the past summer, at the Marine Biolog. Lab., Woods Hole, Mass.: *Cora J. Beckwith*, *A. J. Goldfarb*, *H. B. Goodrich*, *Mildred A. Hoge*, *Louise H. Gregory*, *E. N. Harvey*, *R. R. Hyde*, *Jacques Loeb*, *Max W. Morse*, *Charles Packard*, *A. M. Pappenheimer*, *A. Franklin Shull*, *C. R. Stockard*, *Hardolph Wasteneys*, *Isabel Wheeler*, *L. L. Woodruff*.

**Officers in societies.** Dr. *Carl L. Alsberg* has been appointed secretary of the Assoc. of Official Agric. Chemists.—Dr. *Raymond C. Osburn* has been elected president of the N. Y. Entomolog. Soc'y.—Dr. *Ralph G. Stillman* is president of the Nu Sigma Nu Alumni Assoc. and Drs. *Clinton B. Knapp* and *Wm. K. Terriberry* are members of the exec. commit.—Dr. *Philip Van Ingen* is a member of the Public Health Hosp. and Budget Commit. of the N. Y. Acad. of Med.

**Lectures.** Dr. *Jacob Rosenbloom* recently delivered a lecture before the Scientific Soc'y of the Western Penn. Hosp., Pittsburgh, on the evolution of modern biochemistry. At this institution he is also giving a course of lectures, with demonstrations, on methods for the analysis of urine, feces, stomach contents and breast milk (five lectures), nutrition (ten lectures), and the chemistry of plant and animal life (five lectures).—At the tenth anniversary of the establishment of the Desert Lab. of the Carnegie Institution, which was celebrated at Tucson, Ariz., Sep. 20, Prof. *B. E. Livingston* demonstrated to the visitors, including members of the Intern. Phytogeographic Soc'y, some of the results of his researches, now in progress, on Water relations of plants.—Dr. *F. J. Seaver* delivered one of the "late summer lectures" at the N. Y. Botan. Garden, on Shade trees and their enemies.

**Doctorates.** Miss *Marguerite T. Lee* and Mr. *Sidney Born* recently passed public examinations in final completion of the requirements for the Ph.D. degree at Columbia Univ. The subjects of their dissertations were, respectively, A study of modifications of the biuret test, and The chemical constitution of invertase.

**Miscellaneous items.** Prof. *R. Burton-Opitz* has been elected president of Alpha Omega Alpha, the honorary medical society, which now has chapters in the seventeen leading medical schools.

Miss *Helen Gavin* recently completed the requirements for the M.A. degree in biolog. chemistry at Columbia Univ.

Dr. *A. J. Goldfarb* continued, during the summer at the U. S. Fisheries Marine Biolog. Sta. (Beaufort, N. C.), his experiments on the grafting of eggs, and on changes in organisms produced by chemical means.

Prof. *Wm. H. Woglom* is the author of Vol. I of *Studies in Cancer and Allied Subjects*, conducted under the auspices of the George Crocker Special Research Fund at Columbia Univ. The volume is entitled: *The study of experimental cancer: A review* (1913, pp. 288).

Dr. Rhoda Erdmann, of the dep't of protozoology of the Berlin Inst. for Infec. Dis., has been appointed Seessel research fellow in zoology at Yale Univ., to enable her to study Prof. *L. L. Woodruff's* pedigreed race of *Paramaecium*.

## 2. Proceedings of the Association

The third annual dinner will be given, at the Hotel Marseilles, on November 21. The guest of honor will be Prof. Lafayette B. Mendel, who will address the Assoc. on the results of his studies of Growth. The fourteenth scientific meeting will be held at the Col. of Phys. and Surg., on Dec. 5, at 4 p. m. The proceedings of each of these meetings will be published in the January issue of the BULLETIN.

## 3. Columbia Biochemical Department

**Marriage:** On Sep. 1, Miss Ethel Brand and Dr. Louis E. Wise.

**Resignations from and appointments to the staff.** RESIGNATIONS. Dr. *Max Kahn* (assoc.) has been appointed an assist. in the pharmacol. lab. of the U. S. Bur. of Chem.—Dr. *Louis E. Wise* (instr.), has been appointed instr. in chemistry at the Univ. of Missouri.

APPOINTMENTS. Dr. *Sergius Morgulis*, lately research fellow in the Nutrition Lab. of the Carnegie Inst. (Boston), has been appointed instr., to succeed Dr. Louis E. Wise.—Mr. *Arthur Knud-*

son, who served temporarily as chemist during the summer in the Turck Inst. (N. Y.), has been reappointed to his assistantship in this laboratory.

**Miscellaneous items.** Prof. Gies, on Oct. 11, delivered the second of the nine "autumn lectures" at the N. Y. Botan. Garden in a series on foods, subject: The digestion of vegetable foods. Prof. Gies was associated with Drs. L. H. Baekeland and R. E. Doolittle as an appointed representative of the Amer. Chem. Soc'y in the N. Y. Gen. Commit. for the entertainment of the foreign delegates arriving at the port of New York to attend the Third Int. Congr. on Refrigeration (p. 126).

Volume III of "Studies in cancer and allied subjects, under the auspices of the George Crocker Special Research Fund at Columbia Univ.," was recently issued. It contains reprints of papers from the departments of zoology, surgery, clinical pathology and biolog. chemistry. "Part IV: Dep't of biolog. chemistry," which was edited by Prof. Gies, occupies pages 151-295 and consists of papers by Prof. Gies and Drs. Max Einhorn, S. S. Friedman, Max Kahn, Morris H. Kahn, D. J. Kaliski, Reuben Ottenberg, Jacob Rosenbloom, Charles H. Sanford, and J. W. Weinstein.



## EDITORIALS

The average scientist has often wondered how logic, with that diametrically opposed to it, can together find such a comfortable resting-place in the mental abode of Sir O. Lodge. This renowned **Sir Oliver Lodge** on English man of science, in his recent presidential "Continuity" address before the British Assoc. for the Adv. of Science,<sup>1</sup> advances at one and the same time ideas very plausible and others highly improbable, to say the least.

That the laws of chemistry and physics hold sway in the animate as well as the inanimate world, but that the animate is something more than a mere conglomeration of chemical and physical laws, seems highly consonant not only with reason but with observation. But why Sir Oliver should put faith in psychic phenomena—the study of which thus far has been barren of any tangible result—as a means of supplying the missing link in "continuity," is beyond comprehension.

"Ever since the time of J. R. Mayer," writes Sir Oliver, "it has been becoming more and more certain that, as regards performance of work, a living thing obeys the laws of physics, like everything else; but undoubtedly it initiates processes and produces results that without it could not have occurred—from a bird's nest to a honeycomb, from a deal box to a warship. The behavior of a ship firing shot and shell is explicable in terms of energy, but the discrimination which it exercises between friend and foe is not so explicable. . . . Life introduces something incalculable and purposeful amid the laws of physics; it thus distinctly supplements those laws, though it leaves them otherwise precisely as they were, and obeys them all."

Thus far, thus good! Loeb or Schäfer might be tempted to deny part of this statement, or supplement it, but for most of us it seems to have the ring of truth. But what are we to make of this:

" . . . the facts examined have convinced me that memory and

<sup>1</sup> For a complete account see the *London Times*, Sept. 11, 1913.

affection are not limited to that association with matter by which alone they can manifest themselves here and now, and that personality persists beyond bodily death."

What "facts" is Sir Oliver speaking of? To the scientific world at large these "facts" have thus far proved delusions pure and simple. Not only has not a single "fact" been substantiated, but overwhelming evidence is accumulating daily to show how utterly preposterous are assertions of this kind as to *known* facts.

True, Sir Oliver, there may be more in this world than is dreamt of in our philosophies, but our present methods of studying psychical phenomena give no promise whatsoever of bringing those dreams within range. Our limited vision and our limited capacities are the only weapons with which we can fight life's battles. But limited as we are, need there be any cause for pessimism? Who knows what further evolution in man, as well as further development of the sciences, will bring.

B. HOROWITZ.

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In pursuance of our plan to facilitate open consideration and possible removal of the obstacles in the way of more effective biological organization in this country, we append a few additional **The Mathews plan** quotations from letters on the subject<sup>1</sup> and also **for an American** present, in the succeeding editorial by Dr. Eddy, **Biological Society** a summary of the opinions published in this number, and in the April and July issues of the BULLETIN.

WM. N. BERG, *Bureau of Animal Industry, Washington, D. C.* Most of my thoughts on Dr. Mathews' plan of organizing an Amer. Biolog. Soc'y and of lowering the cost of a collection of journals of biological science have already been expressed by those of your correspondents who oppose the formation of any new organization on the ground that there are societies enough at present. Revision downward, if anything, is wanted. Any further federation of existing biological societies that would result in the benefits of co-operation would naturally appeal to all of us that are interested.

<sup>1</sup> We received a number of letters in which the authors indicated an intention to give the plan mature deliberation before expressing their opinions. In most of these cases the expected comment has not been received.

I am in favor, however, of that part of the plan pertaining to the lowering of the subscription rate on several journals if all are subscribed for at the same time. This would enable an instructor located, let us say, in the middle West or South, whose nearest libraries are of moderate size, to supply himself with the journals he needs. But in so far as men nearer large libraries might find this unnecessary, I believe a vote should be taken so that those who are willing to subscribe to a set of journals can express their wishes in the matter. Speaking for myself—"I couldn't drink another drop."

ULRIC DAHLGREN, *Princeton, N. J.* I would prefer to see the existing Soc'y of Naturalists continued and strengthened and reformed.

LEWIS W. FETZER, *Office of Expt. Stations, U. S. Dep't of Agric., Washington, D. C.* I am of the opinion that the Mathews plan is an admirable one, but the success of the organization can only come through the amalgamation of existing societies. An entirely new organization is an unnecessary evil.

The abstract journal idea is a good one and should receive the generous support of all interested in the biological sciences. To say the least, we are sorely in need of a journal of this character.

Members of the new society should have the option of subscribing to three or more journals, but the abstract journal should always be amongst the minimum number. This would allow investigators with limited finances to subscribe to a few foreign journals. A "Journal of Biological Industries" is needed in this country, but it should not be forced upon all the members of the society.

WILLIAM J. GIES, *Columbia Univ.* I favor the objects of Prof. Mathews' plan. I believe that the logical development of the Federation of Amer. Societies for Exp. Biology, which was organized a year ago and which is in effect an embryonic Amer. Biolog. Soc'y, would secure all the many desirable results at which Prof. Mathews' excellent and far-reaching plan is aimed. The Federation, by a process of evolution, will probably gather into its affiliations all the societies that show *natural* tendencies to cooperation; the constituent societies will be *natural* sections; the obvious economies in the issuance of joint programs and the publication of coordinated pro-

ceedings will suggest others; and the advantages of labile organization of independent societies in *natural* interdependent relationships will impel careful consideration of such additional projects as the evolution of the biological sciences may suggest. I think we should proceed as rapidly as possible in the direction of the Mathews plan through the agency of the Federation—that we should perfect the latter organization and go forward with such further developments as the growth of the Federation might suggest and determine.<sup>1</sup>

PHILIP B. HAWK, *Jefferson Medical College, Phila.* The Mathews plan for the organization of an Amer. Biolog. Soc'y appears to me to have much to commend it.

JOSEPH S. HEPBURN, *Food-Research Lab., U. S. Dep't of Agric., Phila.* While a federation of the various biological societies may be consummated, their complete merger is a rather remote possibility. Thus the chemical engineers, the electrochemists, and the biological chemists have their separate organizations, entirely independent of the Amer. Chem. Soc'y; the biological societies are more numerous than the chemical, and their complete merger would be a more difficult proposition. A membership fee of \$20 or \$30 for the new society would perhaps be prohibitive to many biochemists who are already members of the Amer. Chem. Soc'y, and also pay membership fees in one or more local scientific societies, institutes or academies, in order to gain access to the complete files of scientific journals, foreign and domestic, in the libraries of the latter institutions. Moreover, the average biochemist would constantly use perhaps three, and occasionally perhaps as many more, journals in the list of fourteen; the others would be of very little use to him. In this connection it should be remembered that the Amer. Chem. Soc'y does not supply to its members all of the chemical journals published in the United States. The proposition to grant membership and subscriptions to say any three or four journals out of the list of fourteen for a fee of about ten dollars would doubtless make a strong appeal to the biochemist.

The biological abstract journal is a gigantic undertaking, since it should include, in addition to abstracts of papers in the various branches of botany and zoology, the material now found in the

<sup>1</sup> Editorial: *BIOCHEM. BULL.*, 1913, ii, p. 332.



*Zentr. f. Biochem. u. Biophys., Jahr. über die Fortsch. d. Tierchem.,* and *Centr. f. Bakter., Parasitenk. u. Infektionskr.* The financial burden of publishing such a journal would be so great that it would have to be limited in scope, for instance leaving biochemical abstracts to *Chem. Abstr.*, and thus depriving members of the new society, not subscribers for the latter journal, of abstracts of a large portion of biological science. The financial dilemma might also be solved by converting the new journal into an index of biological literature, which would give the titles but not the subject matter of researches in all the fields of biology.

Local sections of the new society or federation, sufficiently broad in scope, would fill a long-felt need, even in the very large cities; existing local societies might well serve as nuclei which, by a process of expansion, could develop into local sections.

PAUL E. HOWE, *Columbia Univ.* The Mathews plan for the amalgamation of the various existing societies for the promotion of the biological sciences is most attractive as an ideality. The practical attainment of the plan, as suggested, appears feasible. The estimates might be questioned when we consider the budget of the Amer. Chem. Soc'y, with its large membership and the present indication that the membership fee may be increased.

In addition to the advantages of affiliation, the matter of an abstract journal is most attractive. The cost of maintaining such a publication which would be entirely satisfactory, without presuming the use of another to supplement it, would, it seems to me, be much greater than is estimated. One possibility has suggested itself for the reduction of expense and the economical attainment of a satisfactory biological abstract journal: cooperation with the Amer. Chem. Soc'y, so that the members of the biological society would receive *Chem. Abstracts* with its biological section, which would permit the biological society to confine itself to the publication of abstracts in fields not covered by *Chem. Abstracts*. In general I am most heartily in favor of the proposed society with its accompanying advantages.

MAX KAHN, *Bureau of Chemistry, Washington, D. C.* I am fully in accord with Dr. Mathews' plan for the organization of an Amer. Biolog. Soc'y. A Biolog. Abstr. Jour. is a necessity at the



present time. There is no journal that adequately and completely reviews all the current biological literature, and the biologist must himself plod through all the biological journals in the languages which he can read, and trust to luck that in the periodicals which he has not examined there is naught of interest for him in the special biological field that he may be working in. I have had occasion to look through most of the abstract journals in medicine and in chemistry, and I have found them all wanting. The *Jour. of the Royal Micros. Soc'y* omits all papers of biochemical nature, and usually treats only of those biological papers which deal with morphology.

ALFRED P. LOTHROP, *Columbia Univ.* The plan suggested by Prof. Mathews is an admirable one provided the autonomy and organization of the existing societies are preserved in the new organization. In other words the mere payment of dues should include membership in the general society, but the sections (the existing societies) should be entirely free to elect into their membership such members of the general society as can present the qualifications required for membership in the existing societies. A biological abstract journal would be of immense value and the *Biolog. Sect. of Chem. Abstr.* might well be turned over to the management of the proposed "Biological Abstracts." A plan of a scale of fees to include the abstract journal and as many other publications as might be selected would seem to be more feasible than levying dues large enough to include subscriptions to all the journals on the list.

S. S. MAXWELL, *Univ. of California.* I have taken time to give considerable thought to the Mathews plan before expressing an opinion. It now seems clear to me that, notwithstanding the good features of the proposal, the result would be an additional journal and an additional society, and that thus the burden would not be lifted but made heavier.

AMOS W. PETERS, *The Training School at Vineland, N. J.* Any serious consideration of the Mathews plan at once raises several important questions. Is the proposed organization desirable in addition to those now existing, or, if it is to absorb them by what is essentially an extension of the present Federation plan, would it be desirable to extend the process of federation so as to include all biological organizations? In other words, are the unity of inves-

tigative method and the viewpoint of data and the breadth of interest of those who represent widely different subjects, which however all deal with a common living matter—are these sufficiently developed today to hold such an organization together? The native, inherent correlations of these subjects and their irresistible movement towards ultimate quantitative physical and chemical method must come home at times to every investigator in these fields. If the biological subjects shall be held together by one comprehensive organization the bond of union will have to be more effective than that which is represented by our greatest example of combination, the A.A.A.S. Why has the Amer. Chem. Soc'y, our model for the proposed biological society, grown up aside from and after the complete organization of the A.A.A.S.? Are the divisions of biology as now pursued naturally articulated so that the analogy with chemistry holds or would they be conglomerate units so as to be analogous to the A.A.A.S.? The probably correct opinion is that biology as a whole today occupies a middle position in this respect. In the last analysis it is probably largely a question of whether leadership, coöperation and the practical conduct of such an organization can stimulate and maintain the *interest* of its constituents.

The publication of journals is no doubt an important feature of the proposed biological society. A plan for this purpose should be worked out to details without which its feasibility cannot be determined. Perhaps this could be best done after the society had been organized. It seems to me unwise to base the argument for this new society so largely on the journal feature, as this alone or as a principal consideration would not suffice to hold it together. The subject of journals having aroused much responsive interest, the new society should carefully consider the utility and the financial aspects of this part of the proposition.

HOWARD S. REED, *Virginia Agric. Expt. Station*. I am not in favor of the Mathews plan for an organization of biological societies, because I do not think it would bring about the desired results. It is true that we have many societies, but it is equally true that the societies have been organized and developed to meet definite ends. This is an age of increasing specialization, and individual men cannot begin to cover the field of the biological societies today. Ten

years from now the task will be more difficult. Those societies which publish journals, do so to provide for their own technical papers, that is, to have a place where the work of their colleagues will be segregated from other papers of less professional interest. Most scientists with whom I am acquainted, subscribe personally for two or three of the journals dealing most closely with their own work, and depend upon the library of their institution for others of general rather than specific interest. The history of the specialized societies shows that there is a constant tendency to break up the older bodies into smaller, more highly specialized groups, if not to form new societies. Where specialized organizations have merged their identity with large societies, there have usually been formed subsequently new special societies to take the place of those which entered the amalgamation.

I am heartily in sympathy with Professor Mathews' project to unite the biological interests of the country and to make them more effective in the general development of education, and diffusion of biological knowledge; and I am in favor of a scheme of coöperation or affiliation among societies having allied interests. I would like to see the group of biological societies meet annually at the same time and in the same place, to issue a joint program and, wherever possible, to hold one or more joint sessions in which two or more societies might profitably unite, but the range of interest is so great that I do not think they could ever be united into one solid organization.

EDWARD L. RICE, *Ohio Wesleyan Univ.* There is much which attracts in Prof. Mathews' plan for an Amer. Biolog. Soc'y, with its arrangement for increased distribution and support of our scientific journals. But I am tempted to raise a few questions as to its practicability.

1. If it means "one more" society, is it worth while? Or will enough of our present societies disband to make a place for it? At present we never know which society to attend at any particular time.

2. Isn't Prof. Mathews too optimistic as to the support of the society by the biologists of the country? We are many of us pretty badly strapped financially, and unable to accept many offers which we recognize to be good bargains.

3. Would the libraries continue to subscribe at old rates for the journals, or would they depend upon getting them through members of the society and at the society rate?

4. Would it not be better, if practicable, to keep the dues lower and to include part of the journals suggested. Few biologists would be vitally interested in more than about half the journals.

This raising of objections on my part does not mean opposition to the scheme but a desire to see it worked out successfully. I am ready to apply for membership at once.

CARL ALOIS SCHWARZE, *N. J. Agric. Expt. Station, New Brunswick*. If the various biological and chemical societies could, through unification, organize a biological society along the lines of the Amer. Chem. Soc'y, I believe we could bring order out of chaos. I think many biologists would gladly avail themselves of the opportunity to procure a number of scientific publications at club-rates.

E. E. SMITH, *50 E. 41st St., New York City*. The value of Mathews' plan for an Amer. Biolog. Soc'y is determined by what American biologists want. If they want exclusive organizations in which membership is recognition of achievement, then the present organizations meet the requirements. If they want a large organization in which membership is merely recognition of interest and ambition, and whose value is in its strength, then Mathews' plan is an admirable one. That in the main it is practical, it seems to me is demonstrated by similar movements, notably by the history of the Amer. Chem. Soc'y. The argument that it will fail because of the increased expense to the members was put forward by those opposed to the present organization of this latter society; but the argument was not supported by subsequent developments. The whole matter is to be decided by whether exclusive membership or strength in numbers is desired. Each has its advantage. Probably the limited membership is more especially advantageous to the individuals; and strength in organization, to the science as a whole, since it promotes dissemination. Possibly in time this latter would also react to the advantage of the individuals.

EDWIN D. WATKINS, *Univ. of Memphis*. The Mathews plan is a splendid one, and would work toward the same end as the Amer. Chem. Soc'y.



R. M. WEST, *Univ. of Minnesota*. I have followed the discussion of the Mathews plan for the organization of an Amer. Biolog. Soc'y with a great deal of interest. While it is based very largely upon the present organization of the Amer. Chem. Soc'y, it appears to me to differ in one very vital particular. The Amer. Chem. Soc'y journals have been successful largely through the fact that in the two publications which are issued, the articles are of sufficient general interest to encourage chemists in all lines of the science to become members of the society, while *Chem. Abstr.* has of course provided a very thorough review of current literature in all branches of chemistry. According to the Mathews plan, it apparently is the idea to continue the publication of all or nearly all of the present journals in biological science. Even with a clubbing arrangement, the subscription to the number of journals which it would still be necessary to take would be very considerable. If it could be arranged, a much more feasible plan, as it appears to me, would be for a number of the present biological journals to combine to form a nucleus for the proposed society publication. That some such central organization is desirable seems indisputable, and I would be heartily in favor of any plan which would tend to put biological science on the same extensive plane that the Amer. Chem. Soc'y is on at present.

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In the January number of the BIOCHEMICAL BULLETIN, Professor Mathews outlined in detail a plan for the organization of an Amer. Biolog. Soc'y. Shortly after its publication, an invitation to **The Mathews plan:** comment on the plan was forwarded to the members of several of the leading biological societies. **A summary of published opinions** A sufficient number of replies have been published in the BULLETIN<sup>1</sup> to reflect very definitely the views of biologists generally on the subject. We have collated, in this summary, approvals and objections for the convenience of all concerned in further consideration of the matter.

In order that the points of view may be shown clearly in their relation to the plan, the essentials of Professor Mathews' suggestions are recapitulated on the succeeding pages :

<sup>1</sup> BIOCHEMICAL BULLETIN, 1913, ii, pp. 490 and 582; iii, p. 134.



**Plan:** NAME: The American Biological Society.

**OBJECTS:** (*A*) To unite the biological interests for the purpose of mutual support, education, more effective cooperation, defence and encouragement of research, and to increase the influence of biological knowledge; (*B*) to start and support a biological abstract journal; (*C*) to provide new journals as the need arises; (*D*) to diminish to members the cost of dues and journal subscriptions.

**CONDITIONS FOR MEMBERSHIP:** (*a*) All members of present biological societies to be eligible; (*b*) all persons sufficiently interested in biology to pay dues to be eligible; (*c*) local sections to be established with a certain percentage of the dues returned for support; (*d*) present biological societies to organize as sections in the general society (membership in a section might be left to the decision of the section); (*e*) dues to be sufficient to provide each member with the abstract journal and some or all of the biological journals. Professor Mathews estimates that it would be possible to provide an abstract journal and thirteen other journals which cost \$83 for a fee of \$25 per year. The journals he listed (in 1908) were the following: *Amer. Jour. of Physiol.*, *Amer. Jour. Anat.*, *Jour. Compar. Neurol.*, *Jour. of Morphol.*, *Jour. Infec. Dis.*, *Jour. Exp. Med.*, *Jour. Med. Res.*, *Biol. Bull.*, *Jour. Biol. Chem.*, *Jour. Exp. Zool.*, *Anat. Rec.*, *Psychol. Rev.*, and *Botan. Gaz.*

**METHODS OF ORGANIZATION:** (*a*) Either organize the "Naturalists" into a new society or form an entirely new society on lines similar to the Amer. Chem. Soc'y; (*b*) a scale of fees might be presented with an option as to the journals desired; (*c*) the present management of the journals could be retained and a club rate of subscription offered to members of the society; (*d*) the Wistar Inst. might be made the publishing house for the abstract journal and the other journals.

**Objections:** The *principal objections* that have been raised to the scheme may be tabulated as follows:

1. Doubt of the accuracy of the financial estimate submitted. It is believed that the cost of the thirteen journals plus that of the abstract journal would not only exceed Professor Mathews' estimate but so much so as to render the plan unfeasible.

2. Doubt of the financial support of the plan. It is concluded that it would be impossible to secure a sufficient number of members to finance the plan without making the dues and subscriptions prohibitive.

3. Doubt of the possibility of fusion of the existing biological societies. It is suggested that the present members of these societies would resent any attempt to control their present organization.

4. Doubt of the desirability of fusing existing biological societies. It is felt that the present specialization is more desirable than fusion.

5. Doubt of the desirability of making membership open to "any one *interested* in biology." It is assumed that special societies of *workers* are more desirable and effective than general associations with vague qualification for membership and club rates for the reduction of subscriptions for journals.

6. Doubt of the desirability of plans that might mean "merely a new society and a new journal."

7. Doubt of the desirability of a centralization of control for journals. It is considered that better results are obtained when a journal is controlled by workers most interested in the particular subject it represents.

8. Doubt of the desirability of a new abstract journal. It is thought that such a journal would overlap and duplicate the work of existing foreign abstract journals.

**Suggestions.** Aside from the doubts presented above, many offer constructive criticisms and suggestions to obviate difficulties. Some of these are listed below:

A. Suggest a "Federation" similar to that already formed by the Physiological, Biochemical and Pharmacological Societies to control meetings, abstract journals, etc., and at the same time leave to each society its present autonomy and journal control.

B. Suggest the formation of a business organization composed of members of the various societies to finance an abstract journal. This would avoid the necessity of forming a general organization.

C. Suggestions that the division into sections of a general society be based on allied interests rather than on existing societies. This plan would "concentrate" journals, both in content and num-

ber, would lower the subscription rates and would reduce the duplication of printed matter.

D. Suggestion that the membership and subscription fees be graduated with the idea of allowing a member to elect the expense and journals he desires. One plan suggested a \$10 fee to cover dues, abstract journal and an election of two other journals.

E. Suggestion that one of the present "Centralblatts" be made the abstract journal and thus use a medium already established. Addition of financial support and extension of scope would thus be secured at a minimum expense.

**Summary of published opinions.** In the appended summary are indicated the views of those whose opinions have already been published. Under the heading "Objections," the numbers refer to the tabulated objections given above (page 143).

Name	University or other connection	Approval of plan as stated	Objections
Atkinson, Jas. P.	N. Y. City Dep't of Health	Complete	None
Conklin, E. G.	Princeton Univ.	Complete	None
Eddy, W. H.	N. Y. High Sch. of Commerce	Complete	None
Fischer, M. H.	Cincinnati Univ.	Complete	None
Fitz, G. W.	Peconic, Suffolk Co., N. Y.	Complete	None
Gies, William J.	Columbia Univ.	Complete	None
Gortner, R. A.	Carnegie Sta. for Exp. Ev.	Complete	None
Greene, Chas. W.	Univ. of Missouri	Complete	None
Hall, Winfield S.	Northwest. Univ. Med. Sch.	Complete	None
Hawk, P. B.	Jefferson Med. Col.	Complete	None
Houghton, E. M.	Park, Davis & Co., Det., Mich.	Complete	None
Howe, Paul E.	Columbia Univ.	Complete	None
Jackson, D. E.	Washington Univ. Med. Sch.	Complete	None
Jordan, E. O.	Univ. of Chicago	Complete	None
Kahn, Max	U. S. Bureau of Chem.	Complete	None
Koch, F. C.	Univ. of Chicago	Complete	None
Linton, Edwin	Washington and Jef'son Col.	Complete	None
Lloyd, F. E.	McGill Univ.	Complete	None
McClendon, J. F.	Cornell Univ. Med. Sch.	Complete	None
McGuigan, Hugh	Northwest. Univ. Med. Sch.	Complete	None
Moore, A. R.	Bryn Mawr Col.	Complete	None
Osburn, R. C.	N. Y. Aquarium	Complete	None
Parker, G. H.	Harvard Univ.	Complete	None
Schwarze, C. A.	N. J. Agric. Exp. Sta.	Complete	None
Smith, E. E.	50 E. 41st St., N. Y. City	Complete	None
Stewart, Colin C.	Dartmouth Col.	Complete	None
Thorndike, E. L.	Columbia Univ.	Complete	None
Wiley, Harvey W.	Bur. of Foods a. San., Wash.	Complete	None
Watkins, Edw. D.	Univ. of Memphis	Complete	None
Berg, Wm. N.	U. S. Bur. of Anim. Ind.	Qualified	6 <sup>1</sup>
Burnett, Theo. C.	Univ. of California	Qualified	1, 2
Davenport, C. B.	Carnegie Sta. for Exp. Ev.	Qualified	1, 8

<sup>1</sup> Favors a federation.

Name	University or other connection	Approval of plan as stated	Objections
Fetzer, L. W.	U. S. Dep't of Agric.	Qualified	6 <sup>2</sup>
Hargitt, Chas. W.	Syracuse Univ.	Qualified	3
Henderson, V. E.	Toronto Univ.	Qualified	1
Henderson, Yandell	Yale Univ.	Qualified	1, 2
Hepburn, J. S.	Food-Research Lab.	Qualified	2, 3
Hewlett, A. W.	Univ. of Michigan	Qualified	4 <sup>3</sup>
Hoskins, R. G.	Starling-Ohio Med. Col.	Qualified	3
Hough, Theodore	Univ. of Virginia	Qualified	3, 1
Howell, W. H.	Johns Hopkins Univ.	Qualified	4 <sup>4</sup>
Hyde, Ida H.	Univ. of Kansas	Qualified	1, 2
Kingsley, J. F.	Tufts Col.	Qualified	1, 2
Lothrop, A. P.	Columbia Univ.	Qualified	5
Macleod, J. J. R.	Western Reserve Univ.	Qualified	2
McNeal, W. J.	N. Y. Post-Grad. Med. Col.	Qualified	3
Mann, Gustave	Tulane Univ.	Qualified (Suggestions)	
Martin, E. G.	Harvard Med. Col.	Qualified	1
Morse, Max	Univ. of Wis.	Qualified	3
Park, Wm. H.	N. Y. City Dep't of Health	Qualified	3
Pearl, Raymond	Maine Agric. Exp. Sta.	Qualified	3, 5
Peters, Amos W.	Training Sch., Vineland, N. J.	Qualified	3
Reighard, Jacob	Univ. of Michigan	Qualified	2, 7
Rice, Edward L.	Ohio Wesleyan Univ.	Qualified	2, 6 <sup>5</sup>
Rockwood, E. W.	Ohio State Univ.	Qualified	1, 2, 3
Todd, J. L.	McGill Univ.	Qualified	3
West, R. M.	Univ. of Minnesota.	Qualified	1, 2
Wood, F. C.	Columbia Univ.	Qualified	3
Barnhart, J. H.	N. Y. Botan. Garden	Opposed	2, 6
Bergey, D. H.	Univ. of Pennsylvania	Opposed	4, 6
Bigelow, R. P.	Mass. Inst. of Tech.	Opposed	2, 4, 8
Carlson, A. J.	Univ. of Chicago	Opposed	1, 4, 5, 8
Crile, G. W.	Western Reserve Univ.	Opposed	4
Dahlgren, Ulric	Princeton Univ.	Opposed	4
Davis, Bradley M.	Univ. of Pennsylvania	Opposed	2, 4
Dox, Arthur W.	Iowa State Col. Exp. Sta.	Opposed	4
Gager, C. Stuart	Brooklyn Botan. Garden	Opposed	4
Hanzlik, Paul J.	Western Reserve Univ.	Opposed	2, 4, 8
Langworthy, C. F.	U. S. Dep't of Agric.	Opposed	4
Maxwell, S. S.	Univ. of California	Opposed	6
Pearce, Richard M.	Univ. of Pennsylvania	Opposed	4
Reed, Howard S.	Virginia Agric Exp. Sta.	Opposed	4
Sollmann, Torald	Western Reserve Univ.	Opposed	4

## SUMMARY OF THE VOTE:

Total number voting .....	73
Complete approval .....	29
Qualified approval .....	29
Opposed .....	15
Objection 1 raised by .....	11
Objection 2 raised by .....	14
Objection 3 raised by .....	12

<sup>2</sup> Approves the abstract-journal plan.<sup>3</sup> Favors a federation.<sup>4</sup> Favors a society to finance the proposed abstract journal.<sup>5</sup> Hopes to see the plan consummated.



Objection 4 raised by .....	15
Objection 5 raised by .....	3
Objection 6 raised by .....	6
Objection 7 raised by .....	1
Objection 8 raised by .....	4

While it is admittedly not permissible to base sweeping conclusions upon a vote of only seventy-three individuals, yet these individuals are fully representative of the workers in the biological sciences, and in general they approve the plan. A classification of the objections shows that, aside from the doubt regarding the financial estimate and support, the most important objections are those to the fusion of existing biological societies. In fact these are the important objections, for the first two can be established only by a general canvass of the situation, while the latter threaten the plan in its inception. The question then arises: Can these essential objections be met? The summarized suggestions are instructive in this particular: A federation instead of a general society; a special business organization to finance the proposed abstract journal; autonomy for the biological societies as the constituent sections. Such suggestions are valuable for the formulation of opinion, but are not decisive until supported by numbers sufficient to afford a working basis for organization.

The views already expressed stimulate thoughts of more effective organization and should be conducive to that end. The BIOCHEMICAL BULLETIN suggests that at the next annual meetings of the biological societies, free discussion of this entire matter be included in the order of business of each section and that the results of this discussion, together with the vote of each society on the evolved plan, be formulated by the respective secretaries and sent to the BULLETIN for publication in its January issue. The coördinated conclusions might serve as a dynamic basis for the future. Reprints of this summary would be furnished to societies upon request. The BULLETIN is anxious to assist in every way to a concrete conclusion in the matter.

WALTER H. EDDY.

---

The dogmatism of experience is a most dangerous clog to scientific progress.—*Dunning*.



The keenest test of a man comes when he has attained ; the struggle to attain keeps him strong, but the line of least resistance soon shows itself in success.—*Black.*

He that greets Hardship on the threshold of youth may find her a cruel taskmistress, but still a friend. For it is her peculiar function to act as a nurse to the potential conqueror, that he may in the end overcome her and turn her out of doors. Her discipline is rigorous, but they that in good time show her the door are a hardy breed.—*Al K. Li.*

Indifference to the magic of work, the potency of drudgery, is the curse of too many college men. They want to fly before they can creep; they want to be ten thousand dollar men before they are thirty-cent apprentices. Not even college can teach the faculty of absorbing worldly wisdom as a sponge drinks water. Worldly wisdom is a slow growth. You can't get it in the circus of society or the pantomime of sport; you can't get it in the frivolities of pleasure or the steeplechase of mirth; but you can get it in a man's work among men and nowhere else.—*Glynn.*

The study of recent literature forces from us the question, why so many students of the (chemical) science, leaving of course the workers in color chemistry and in the synthesis of alkaloids out of account, regard themselves as in duty bound to study the products of the distillation of coal, the relics of a long extinct organic world, and their derivatives, instead of turning their attention to the living world which surrounds them. To invent new methods and to follow their application in this region would surely not be less interesting than the piling up of many-membered rings.—*Lassar-Cohn.*

The meat of success is savorless without the salt of content. To him that cannot look upon his treasures and the work of his hands and say in his innermost conscience, "It is good," there is no success. Monumental achievements only madden by their futility if they lack the approval of the still, small voice. In the last analysis the human struggle is one for self-approval. The problem of self-preservation is readily solved by the majority of mankind. It is elemental and comparatively easy. But the problem of winning self-approbation—not the self-approbation of the shallow egotist, but that of the wise, level-headed, introspective person—is elemental and stubborn. He who has solved it is favored of the gods.—*Em. Phatic.*

## BOOKS RECEIVED

The BIOCHEMICAL BULLETIN promptly acknowledges here the receipt of publications presented to it. Reviews are matter-of-fact statements of the nature and contents of the publications referred to, and are intended *solely to guide possible purchasers*; the wishes or expectations of publishers or donors of volumes will be disregarded, if they are incompatible with our convictions regarding the interests of our colleagues. *The sizes of the printed pages are indicated, in inches, in the appended notices.*

**Untersuchungen über Chlorophyll: Methoden und Ergebnisse.** By Richard Willstätter and Arthur Stoll, Kaiser Wilhelm Inst. für Chemie. Pp. 424— $7\frac{1}{4} \times 4\frac{1}{4}$ ; M. 20.50. Julius Springer, Berlin, 1913.

This comprehensive volume presents unpublished data, obtained by Willstätter and his pupils in recent years, on the isolation and hydrolysis of chlorophyl and the separation and quantitative determination of its component radicals. A complete compilation and revision of the essential data of Willstätter's classical studies on chlorophyl is included, and the relationship of chlorophyl and hematin is further clarified. The volume is encyclopedic in scope and presents the methods so clearly that it may be used as a laboratory handbook on chlorophyl. That it will aid and stimulate research on chlorophyl is certain and should be studied by biochemists generally. The volume is beautifully illustrated with eleven plates, which indicate details of the crystalline and spectral characters of the products. The work on which the book is based was a monumental achievement.

Gies.

**The elements of the science of nutrition.** By Graham Lusk, prof. of physiology, Cornell Univ. Med. Col. Second ed. Pp. 402— $6\frac{1}{2} \times 3\frac{3}{4}$ ; \$3.00 net. W. B. Saunders Co., Phila., 1909.

This widely appreciated volume, by a master of the subject in both its theoretical and practical phases, is one of the best on nutrition. We use it freely in our advanced courses, and await impatiently the appearance of the third edition.

Gies.

**Nutritional physiology.** By Percy G. Stiles, assist. prof. of physiology, Simmons Col.; instr. in physiology and personal hygiene, Mass. Inst. of Tech., Boston. Pp. 271— $6 \times 3\frac{1}{2}$ ; \$1.25 net. W. B. Saunders Co., Phila., 1912.

An admirable treatment of nutrition, which is very appropriately dedicated to the author's teacher, Prof. Graham Lusk. The chemical phases of physiology are concisely though none the less effectively considered; and nutrition is presented from the *dynamic* point of view without confusion with food chemistry. A very valuable addition to the growing supply of textbooks in biological chemistry for beginners.

Gies.

**Essentials of pathological chemistry, including description of the chemical methods employed in medical diagnosis.** By Victor C. Myers and Morris S. Fine, prof. and instr. in path. chemistry, respectively, at the N. Y. Post-Grad. Med. Sch. and Hosp. Reprinted from the *Post-Graduate*, 1912-13. Pp. 137— $7 \times 4$ ; \$1.25. Post Graduate (Med. Jour.), N. Y. City, 1913.

A very useful compilation of laboratory methods in the pathological chemistry of digestion and excretion, also of milk and blood, with an appendix of laboratory suggestions. The discussions are practical in guidance and broad in interpretation. The book is a very handy laboratory manual. We hope the authors will carry it through numerous revisions and extensions, as the science advances and methods multiply.

Gies.

# Books received (con.)

**Modern research in organic chemistry.** By F. G. Pope. Pp. 324—6 × 3½; \$2.25 net. D. Van Nostrand Co., New York, 1913.

Restricted, with interesting historical introduction, to chapters successively on polymethylenes; terpenes and camphors; uric acid (purin) group; alkaloids; relation between color and constitution of chemical compounds; salt formation, pseudo-acids and bases; pyrones; ketens, ozonides, triphenylmethyl; and the Grignard reaction. Masterly treatment of each subject. Constitutional formulas used freely and effectively. Gies.

**An introduction to the chemistry of plant products.** By Paul Haas (lecturer on chemistry, Royal Gardens, Kew) and T. G. Hill (reader in vegetable physiology, Univ. of London). Pp. 401—4 × 7; \$2.25 net. Longmans, Green and Co., 1913.

Excellent discussion of the chemistry and biological significance of many of the most important plant constituents. Besides extended treatment of carbohydrates, lipins and proteins, chapters are devoted respectively to glucosides, tannins, pigments, nitrogenous bases (alkaloids, ptomaines, purins), colloids and enzymes. Methods of preparation, detection and quantitative determination are numerous and well described. Good *subject* index. The most valuable recent contribution of its kind to phyto-chemistry. Strongly recommended to biological chemists generally—to botanists in particular. Gies.

**Practical physiological chemistry.** By Sidney W. Cole, demonstrator of physiology, Trinity College, Cambridge. Third edition. Pp. 230—4 × 6½; 7s. 6d. net. W. Heffer & Sons, Ltd., Cambridge, Eng., 1913.

Very useful laboratory manual. Subject treated chiefly from static point of view. Practical throughout. Methods well selected. Quantitative procedures given satisfactory attention. Special emphasis laid upon Folin's microchemical methods of urinary analysis. Good index. See review by Walter Jones, *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 1064. Gies.

**Reagenzien-Verzeichnis** enthaltend die gebräuchlichen Reagenzien und Reaktionen, geordnet nach Autorennamen. Dritte Aufl. By E. Merck. Pp. 446—8¾ × 5½. Julius Springer, Berlin, 1913.

Very useful in a biochemical laboratory. References to original literature with description of each reagent or test. Arrangement favors easy reference to desired author, substance or procedure. Gies.

**Annual report of the Virginia Polytech. Inst. Agric. Expt. Station for 1911 and 1912.** 1913 (13 original papers).

**Studies from the department of physiology, Cornell Univ. Med. Col., II.** 1913. (12 reprints.)

**Sloane Hospital for Women (N. Y. City): Obstetrical and gynecological reports.** Vol. I, 1913. Edited by Wilbur Ward. 1913.

**Radium: A monthly journal** devoted to the chemistry, physics and therapeutics of radium and other radioactive substances. Vol. I began with issue in April, 1913. Radium Publishing Co., Pittsburgh, Pa.

**Researches in biochemistry** conducted in the Johnston Laboratory, Univ. of Liverpool. Edited by Benjamin Moore, Johnston prof. of biochem., and Owen T. Williams, demonstrator of biochem. Vol. II; 1908-1911. (27 reprints.)

**Glycosuria and allied conditions.** By P. J. Cammidge. Pp. 467—4 × 6¾; \$4.50 net. Longmans, Green & Co., New York; Edward Arnold, London, 1913.

**The chemical constitution of the proteins: Part II, Synthesis, etc.** 2d ed. (One of the *Monographs on Biochemistry*.) By R. H. A. Plimmer, Univ. reader and ass't prof. of physiological chem., University Coll., London. Pp. 107—4¾ × 7½; \$1.20 net. Longmans, Green & Co., 1913.

## OFFICERS OF THE COLUMBIA BIOCHEMICAL DEPARTMENT\*

Sixteenth year: 1913-'14

OFFICIAL REGISTER, SEPTEMBER 31, 1913

WILLIAM J. GIES: *Professor and Executive Officer*; Consulting chemist, New York Botanical Garden; Pathological chemist, First Division, Bellevue Hospital; Member of the Faculties of N. Y. Teachers College and N. Y. College of Pharmacy. [B.S., Gettysburg College, 1893 and M.S., 1896; Ph.B., Yale University, 1894 and Ph.D., 1897. Instructor, 1898-'02; adjunct professor, 1902-'05; professor, 1905-.]

PAUL E. HOWE: *Assistant Professor and Secretary of the Staff*. [B.S., University of Illinois, 1906; A.M., 1907 and Ph.D., 1910. Assistant Professor, 1912-.]

ALFRED P. LOTHROP: *Associate and Chairman of the Staff*. [A.B., Oberlin, 1906 and A.M., 1907; Ph.D., Columbia, 1909. Assistant, 1908-'09; instructor, 1909-'12; associate, 1912-.]

EMILY C. SEAMAN: *Instructor*. [B.S., Adelphi College, 1899; A.M., Columbia, 1905 and Ph.D., 1912. Tutor, 1909-'10; instructor, 1910-.]

WALTER H. EDDY: *Associate*. [B.S., Amherst College, 1898; A.M., Columbia, 1908 and Ph.D., 1909. Assistant, 1908-'10; associate, 1910-.]

HERMAN O. MOSENTHAL: *Associate*; Assistant Attending Physician, Presbyterian Hospital; Assistant Physician, Vanderbilt Clinic; Instructor in medicine. [A.B., Columbia, 1899 and M.D., 1903. Assistant, 1908-'09; instructor, 1909-'12; associate, 1912-.]

MAX KAHN: *Associate*; Director of the chemical and physiological laboratories, and consulting physician in dietetics, Beth Israel Hospital. [M.D., Cornell University Medical College, 1910; A.M., Columbia, 1911 and Ph.D., 1912. Instructor, 1912-'13; associate, 1913-.]

FREDERIC G. GOODRIDGE: *Instructor*. [A.B., Harvard University, 1897; M.D., Columbia, 1901. Assistant, 1912-'13; instructor, 1913-.]

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CHRISTIAN SEIFERT: *Laboratory assistant*, 1898-.

STELLA WALDECK: *Recorder*, 1908-.

VICTOR E. LEVINE: *Laboratory assistant*, summer session, 1913. [A.B., College of the City of New York, 1909; A.M., Columbia, 1911.]

\*The work of the department was inaugurated in October, 1898, by Prof. R. H. Chittenden (lecturer and director), Dr. William J. Gies (instructor), Messrs. Alfred N. Richards and Allan C. Eustis (assistants), and Christian Seifert (laboratory assistant).



## COURSES OFFERED BY THE BIOCHEMICAL DEPARTMENT OF COLUMBIA UNIVERSITY, 1913-'14

(*Abbreviations:* C, conference; D, demonstration; L, lecture; Lw, laboratory work; R, recitation. Odd numbers indicate the first-half, even numbers the second-half, of the academic year; double numerals indicate full academic year. Courses indicated by numerals in parentheses are not offered during 1913-'14.)

### ORGANIC CHEMISTRY

51. ELEMENTARY ORGANIC CHEMISTRY. (*Medical School.*) Introductory to course 101 or 102. (*Required of first year students of medicine.*) L, D, R, 2 hr. Lw, 6 hr., each section (2). Profs. Gies and Howe, Dr. Lothrop and Messrs. Knudson and Perlzweig.

### NUTRITION (PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY)

61-62. CHEMISTRY OF NUTRITION. (*School of Pharmacy. Required of candidates for the Degree of Doctor of Pharmacy.*) L, 1 hr. Prof. Gies.

101 or 102. GENERAL BIOLOGICAL (PHYSIOLOGICAL) CHEMISTRY. *A course in the elements of normal nutrition. (Full course.)* Given at the College of Physicians and Surgeons, and at Teachers College.

#### COLLEGE OF PHYSICIANS AND SURGEONS—

*Faculty of Medicine (primarily):* 102—"Nutrition (physiological chemistry) 52." Required of first year medical students. (*Second half year.*) L, R, D, 2 hr.; Lw, 6 hr., each section (2). Profs. Gies and Howe, Dr. Lothrop and Messrs. Knudson and Perlzweig. (*Also given during the last summer session by Prof. Gies and Messrs. Perlzweig and Levine.*)

*Faculty of Pure Science (solely):* 101—"Biological chemistry 101." (*First half year.*) L, R, 1 hr.; Lw, 7 hr. Prof. Howe, Dr. Eddy and Messrs. Knudson and Perlzweig.

#### TEACHERS COLLEGE—

*School of Practical Arts:* 101 or 102—"Chemistry 51" and "Household Arts Education 125." L, 2 hr.; R, 1 hr., each section (2); Lw, 5 hr., each section (2). (*Each half year.*) Prof. Gies, Dr. Seaman, and Misses Wickwire and Harkey. (*Also given during the last summer session by Prof. Gies, Dr. Seaman and Miss Harkey.*)

201-202. ADVANCED PHYSIOLOGICAL CHEMISTRY, INCLUDING METHODS OF RESEARCH IN NUTRITION. (*Full course. Teachers College, School of Practical Arts.*) L, 1 hr. Lw, 7 hr. Dr. Seaman and Miss Harkey. (This course is designated "Household Arts Education 127" in the Teachers College Announcement.)

204. GENERAL PATHOLOGICAL CHEMISTRY. *Lectures on nutrition in disease. (Teachers College, School of Practical Arts.)* L, 1 hr. Prof. Gies. (This course is designated "Chemistry 52" in the Teachers College Announcement.)

211-212. BIOCHEMICAL METHODS OF RESEARCH, INCLUDING CLINICAL METHODS AND URINARY ANALYSIS IN GENERAL. (*Full course. Medical School.*) L, 1 hr. Lw, 7 hr. Profs. Gies and Howe, Dr. Eddy, and Messrs. Knudson and Perlzweig.

(213-214) BIOCHEMISTRY OF CARBOHYDRATES, LIPINS, PROTEINS AND ENZYMES. (*Full course. Medical School.*) L, 1 hr. Lw, 7 hr. Prof. Gies.

221-222. NUTRITION IN HEALTH. *A laboratory course in advanced physiological chemistry. (Double course. Medical School.)* L, 2 hr. Lw, 14 hr. Profs. Gies and Howe, and Dr. Morgulis.



### Courses in Nutrition (continued)

223-224. NUTRITION IN DISEASE. *A laboratory course in advanced pathological chemistry. (Double course. Medical School.)* L, 2 hr. Lw, 14 hr. Prof. Gies.

225-226. NUTRITION IN DISEASE. *(Medical School.)* L, 1 hr. Profs. Gies and Howe, and Drs. Mosenthal and Goodridge.

251-252. ADVANCED PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY, INCLUDING ALL PHASES OF NUTRITION. *(Double course. Medical School.)* Research. C, 1 hr. (individual students). Lw, 16 hr. Profs. Gies and Howe, and Dr. Lothrop.

### TOXICOLOGY

261-262. EFFECTS AND DETECTION OF POISONS, INCLUDING FOOD PRESERVATIVES AND ADULTERANTS. *(Full course. Medical School.)* Lw, 6 hr. Prof. Gies.

### BOTANY

271-272. CHEMICAL PHYSIOLOGY OF PLANTS. *(Full course. New York Botanical Garden or Medical School, or both.)* L, 1 hr. Lw, 7 hr. Prof. Gies.

### BACTERIOLOGY

(281-282) CHEMISTRY OF MICROORGANISMS: FERMENTATIONS, PUTREFACTIONS AND THE BEHAVIOR OF ENZYMES. *An introduction to sanitary chemistry. (Full course. Medical School.)* L, 1 hr. Lw, 7 hr. Prof. Gies.

### SANITATION

291. SANITARY CHEMISTRY. *(Half course. Teachers College, School of Practical Arts.)* L, 1 hr. Lw, 3 hr. Dr. Seaman and Miss Harkey. (This course is designated "Chemistry 57" and "Household Arts Education 129" in the Teachers College Announcement.)

### BIOCHEMICAL SEMINAR

301-302. BIOCHEMICAL SEMINAR. *(Medical School.)* 2 hr. Prof. Gies.

### RESEARCH IN BIOLOGICAL CHEMISTRY

Biochemical research may be conducted, by advanced workers, independently or under guidance, in any of the departmental laboratories.

### LABORATORIES FOR ADVANCED WORK IN BIOCHEMISTRY

The laboratories in which the advanced work of the biochemical department is conducted are situated at the College of Physicians and Surgeons, Teachers College, New York Botanical Garden and Bellevue Hospital. Each laboratory is well equipped for research in nutrition and all other phases of biological chemistry.

### BIOCHEMICAL LIBRARY

Prof. Gies' library occupies a room adjoining the main biochemical laboratory at the College of Physicians and Surgeons and is accessible, by appointment, to all past and present workers in the Department. The library contains 2600 volumes and 7000 classified separates.

### COLUMBIA UNIVERSITY BIOCHEMICAL ASSOCIATION

The Biochemical Association holds scientific meetings regularly on the first Fridays in December, February and April, and on the first Monday in June. These meetings are open to all who may be interested in them.

### SUMMER SCHOOL COURSES

See references to courses 101 and 102.

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The BIOCHEMICAL BULLETIN is a quarterly biochemical review. It publishes results of original investigations in biological chemistry, miscellaneous items of personal and professional interest to chemical biologists, original contributions to research, preliminary reports of investigations, abstracts of papers, addresses, lectures, criticism, reviews, descriptions of new substances, methods and apparatus, practical suggestions, biographical notes, historical summaries, bibliographies, quotations, questions, news items, proceedings of societies, personalia, views on current events in chemical biology, etc.

*Subscription prices.* Vol. I: \$6.00 (No. 1, \$1.50; No. 2, \$2.50; No. 3, \$2.00; No. 4, \$1.50). Vol. II: \$5.00 (No. 5, \$2.00; No. 6, \$1.50; No. 7, \$2.00; No. 8, \$1.00). Vol. III: \$2.75 (domestic); \$3.00 (foreign); \$5.00 after July 1, 1914.

Address remittances, manuscripts and correspondence to the Managing Editor, William J. Gies, 437 West 59th St., New York.

# Biochemical Bulletin

Edited, for the Columbia University Biochemical Association, by the

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## DINNER TO HENRY HURD RUSBY

The Alumni Association of the College of Pharmacy of the City of New York honors Dean Rusby

The eighteenth annual dinner of the Alumni Association of the N. Y. College of Pharmacy was given at the Chemists' Club, New York, on December 17, 1913, in commemoration of the twenty-fifth anniversary of Dean Rusby's appointment to the faculty of the College. The dining room was filled to its capacity with a happy company of alumni and other friends of Doctor Rusby.

Toward the close of the dinner Dr. Joseph Weinstein, president of the Alumni Association, addressed the gathering, saying: "It is with a feeling of pleasure that I remind the diners that we have assembled to celebrate the silver jubilee of our beloved dean, Henry H. Rusby. I call upon all present to join with me in paying a tribute to and in felicitating the dean." Dr. Weinstein then introduced Professor Curt P. Wimmer, the chairman of the dinner committee, as the toastmaster. Dr. Wimmer said that no one "outside the family" had been invited to speak on this occasion, because the dinner committee felt that everything should go the "Rusby way," which is a simple way, but a way of results and achievements.

After reading a number of letters from distinguished pharmacists who were unable to be present, the toastmaster introduced Professor William H. Carpenter, Provost of Columbia University, who said in part:

"I feel profoundly grateful that the chairman has classed me as a member of the great and harmonious family of the College of Pharmacy. I was somewhat shocked when I received the invitation to attend this dinner because it was stated to be the twenty-fifth

anniversary of Dean Rusby's connection with the College of Pharmacy. I can not think of Dean Rusby as of an age that a twenty-fifth anniversary would seem to indicate, for he has none of the characteristics that we are apt to regard as the characteristics of age. In clearness of vision, in mind and in heart he is young and he will always remain young no matter what the measure of his years may be.

"I came here to-night to represent the University and to lay my tribute at this twenty-fifth milestone which marks the broad highway of the Dean's progress through life. I value my association with Dr. Rusby. I know of his scientific accomplishments, of the depth and the breadth of his influence in that great field in which he is a laborer. We of Columbia value our connection with the College of Pharmacy as one of the great and important parts of the University. The College of Pharmacy has grown in size and in influence on account of the realities of its purposes and its achievements and on account, too, of the wise administration of its dean.

"Dr. Rusby is a 'bonny fighter.' He has fought a sturdy, valiant and honest fight for higher educational standards in pharmacy. He has contributed in no small part to make the pharmacist more and more a powerful influence for good in the community. He has helped to make the profession of pharmacy one of the important members in the whole group of the learned professions. Happy is the university that has such a man among its teachers! Thrice happy is that department of our University to have as its leader a man of such wide horizon, such high ideals, such steadiness of purpose and serenity of soul. May Dean Rusby live long and may he enjoy the deserved fruits of his labors."

Dr. Charles F. Chandler then addressed the association: "Dr. Rusby is one of my boys. I don't remember him as one of my students, since I knew intimately only the tail-enders of the class. Professor Rusby should be a happy man—first, because he has been a teacher all his life; second, because he is sympathetic with and interested in his students. My first real acquaintance with Dr. Rusby began when he joined the faculty of the College of Pharmacy. When Dean Rusby lectures to the students he impresses them with the fact that he knows what he is talking about. This is

a great asset to a teacher. I don't think he has a superior, and I am sure he has few equals as a teacher. Since Dean Rusby has been connected with the college it has prospered. Each year new courses have been added, new members added to the faculty, and new facilities provided for the students. This has resulted in an increased attendance. In conclusion, I hope Professor Rusby will be here to celebrate his half-century with the college."

Dr. William J. Schieffelin said: "It is an anti-climax for me to follow Professor Chandler. When I returned from Munich in 1889 I knew Professor Rusby as a slender, curly-haired young man. We, the trustees, are always able to bank on Professor Rusby. In order to secure pure drugs he penetrated the wilds of South America and Mexico. In later years he has continued the fight for pure drugs. It is great to feel that we have scientific men who care for truth. Dr. Rusby has stood like a rock for the highest standard of purity in drugs. I am proud to have been connected with him, and with the trustees of the College of Pharmacy.

Dr. George C. Diekman said in part: "It will be impossible for me to say one-half of that which I have in mind to say concerning the one we have come here to honor this evening, and who completes this year twenty-five years of uninterrupted, capable, honorable and faithful service to our college. How efficient these services have been, and how faithfully they have been performed, is not only known to every member of our faculty, but to everyone connected with the college as well. It is really my good fortune to have the opportunity of addressing those here assembled concerning one about whom so much that is good can with truth be said. Professor Rusby is so well known to all present that my further remarks concerning him will, I am certain, be endorsed in every detail.

"During my long and at all times pleasant and cordial association with Dean Rusby two qualities of the man have impressed themselves upon me more than any others. They are honesty of purpose and unselfishness. I need say nothing here concerning his many other admirable qualities, nor about his reputation as a scientist and teacher. A correct estimate of the two qualities referred to can only be made in case of any man, after long-continued asso-

ciation and study and observation at close range, and such have been my opportunities in this case.

"I know of no one who is more honest of purpose than is Professor Rusby. Nothing can induce him to withdraw when once he has decided to lend his influence to any cause. He has on many occasions entered into a contest against long-established customs and abuses, or a contest against individuals, when it would have been greatly to his advantage to have remained neutral, or at least to have fought less vigorously and persistently. In many like situations a man less honest in purpose would have withdrawn from the contest when once it became clearly apparent that in gaining victory in a contest for principle he was to be personally a loser. Dean Rusby could not, even if he desired, say one thing and do another. Once he has satisfied himself that he is right he proceeds to act regardless of his own personal interests.

"And now, Dean Rusby, I come to the most pleasant part of that which I am privileged to do here to-night. You already are aware of the high esteem in which you are held by the members of the faculty. Nothing can add or take from that esteem. And in order that you may be reminded, if indeed a reminder is necessary, of the very cordial and fraternal relations which exist between yourself and the members of the faculty (and I am using the term faculty in its broadest sense), when you are at home and away from the scene of your labors, the members of the faculty decided to present you with a tangible evidence of their love and affection in the form of the loving cup I now have the honor to place in your hands.

"We feel and know that you will prize the sentiment which prompts and accompanies the gift far more highly than its intrinsic value. We ask you to accept it as a token of fidelity and loyalty, which will endure as long as we are permitted to labor together for the honor and glory of our grand old institution, the College of Pharmacy of the City of New York. God bless you."

Dr. Rusby said, in accepting the loving cup: "As I sat and listened to the different speakers I felt that I had much to say. But after receiving this beautiful gift, words go from me. It is difficult to reply. As I have listened to the different things said



about me I have pinched myself to see if I were alive. Such pleasant things are usually said about a man after he is dead. You have all heard what I have done for the college. What has this college done for me? It has moulded and built my soul. I have profited by my association with the other members of the faculty and with the trustees. I have grown in character each year of my association with the college. In my work as dean of the college I have been brought closely in contact with the worst elements of the various classes. Instead of removing these men from the college I have admonished them and saved them from themselves. The College of Pharmacy is not a one-man college; it is a college of growth. It is a college which always does what it says it will do. The spirit of harmony is the dominant note in the College of Pharmacy."

Mr. Thomas Main, in speaking for the alumni association, said in part: "I was one of the signers of the petition to form an alumni association. The other signers were: P. W. Bedford, class of 1858; D. C. Robbins, class of 1836; William Hegeman, class of 1837; E. L. Milhau, class of 1856; C. B. Smith, class of 1863; Theobald Frohwein, class of 1863; J. W. Ballard, class of 1870; Edwin Henes, class of 1871. The call was sent out on May 10, 1871. Six of the nine signers have now passed away. Those left are John W. Ballard, who, having had a successful drug store in Davenport, Ia., for many years, is now a banker; his drug store is now conducted by one of his sons under the name of the Ballard Drug and Dental Company. The other two survivors are Edwin Henes, of this city, and myself. P. W. Bedford played a most important part in forming the association. He not only signed the call but by his influence obtained the names and secured the influence of the signers, and I strongly suspect was instrumental in influencing D. C. Robbins, of the class of 1836, who was then considered the Nestor of the wholesale drug trade not only of New York, but also of the entire United States. He accepted the presidency of the new association for the first two years of its existence, which insured its success from the start.

"Mr. President, I venture to think that one of the things the Alumni Association may well be proud of is the part it took in



introducing our dear friend and guest of the evening, Dr. H. H. Rusby, to its members and the members of the College. Dr. Rusby, during 1885 and 1886, had been engaged in an exploring and botanizing expedition which led him from the western coast of South America across the Andes and from the sources of the great river Amazon to the Atlantic Ocean. In February, 1888, he was introduced to an audience composed of members of this Association, members of the College and to other scientific societies, by Chas. F. Heebner, then president of this Alumni Association, when Dr. Rusby gave a graphic account of his journey with its scientific results. Dr. Rusby's lecture created a profound impression at that time and I believe resulted in his appointment to the Chair of *Materia Medica* and Botany in the following year.

"With the advent of Dr. Rusby as Professor in our College came his 'object lesson' methods of teaching his subjects, which have been so successful as to compel a complete revolution from former methods of teaching *materia medica*, not only in our own institution, but in all other Schools of Pharmacy that consider themselves up-to-date.

"The year 1914 will mark the 25th year of Dr. Rusby's connection with our institution. He is now our senior Professor in active service, and Dean. During all these years he has given his best energies and his best thought to his work in the College, and has been a most important factor in placing and maintaining the College of Pharmacy of the City of New York in the proud position it holds to-day among the schools of pharmacy of the United States and of the world.

"As the first lecture of Dr. Rusby in our College was delivered upon the invitation of the Alumni Association, it seems eminently proper that this Association should be the first to congratulate him upon the near completion of his twenty-five years of important service in the College. Mr. Dean, you are here to-night as our honored guest, and it is my great privilege on behalf of the Alumni Association to present you with this silver set, tendered as an appreciation of your long, honorable and valued service to our beloved alma mater. During this time you have done your duty as you saw it, without fear or favor, and have earned the friendship and high esteem of all our members."

In conclusion, the toastmaster expressed the hope that the dinner had served to show the Dean the love and affection which his colleagues and old students feel for him, and to voice the respect and esteem in which he and his work are held by all who know him.

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## VIEWPOINTS IN THE STUDY OF GROWTH<sup>1</sup>

LAFAYETTE B. MENDEL

From whatever standpoint the student of science considers living organisms he soon learns that there are certain fundamental characteristics peculiar to their protoplasm and distinguishing it from what is commonly termed unorganized matter. Life without growth and activity, without the power of "automatic development, self-preservation, and reproduction," is at present inconceivable. Whether or not the artificial production of living matter from that which is lifeless may some day be accomplished need not concern us now. As Karl Pearson has written: "There is mystery enough here, only let us clearly distinguish it from ignorance within the field of possible knowledge. The one is impenetrable, the other we are daily subduing."

I have termed the subject of this review "viewpoints" to emphasize what is all too frequently forgotten, namely, that the data of science are continually changing as the result of the addition of new facts and the modification of the known. Such changes bring with them new sequences—they compel us to new conclusions and suggest new inquiries. Donaldson recently remarked that: "The attitude toward knowledge during our student days is almost necessarily such as to throw the idea of change into the background and unduly emphasize the permanency of the things taught. The facts are otherwise" (*Science*, July 25, 1913, p. 109.) Furthermore, it is quite as important for the scientific investigator to formulate clearly the problems which his experience dictates as to be concerned solely with his experimental researches. (I confess, however, that I often feel sympathy with a remark attributed to the late Professor Atwater, that his idea of a scientific man's heaven

<sup>1</sup> This paper was read in part at the third annual dinner of the Columbia University Biochemical Association in New York City, November 21, 1913; subsequently, also, before the local chapters of the Society of the Sigma Xi at the University of Kansas, the University of Missouri, and Washington University, St. Louis. The charts and photographs are not reproduced here.

was a place where one could work incessantly without the necessity of preparing one's results for publication.)

It is surprising that in comparison with other topics of physiological study so little has been published in the past about growth; and much of what has been written invades the domain of hypothesis and speculation. Together with inheritance, growth provides for the permanence of the various external manifestations of life. The problems of agriculture—the production of the plant products from the soil and animal husbandry—are based upon considerations of growth. I need scarcely add that it would be of immense direct importance to man and to medicine to know more about “the regulatory power which presides over growth,” so that we might derive more practical applications of the discoveries in this field. In ultimate analysis all of our material prosperity, indeed, the very possibility of the maintenance of the race, depends upon the manifestation of growth.

The dominating viewpoint in the consideration of the phenomena of growth will be determined in large degree by the training and immediate interest of those engaged in the analysis thereof. Some investigators—and these represent by far the largest group—have directed their attention to the purely morphological aspects of the subject. Cytological phenomena, the changes in the number and size of the body cells, the interrelation of the tissue components, the comparative proportions of nucleus and cytoplasm, and similar *structural* differentiations have engrossed their interest. Others, again, have encompassed the problems of growth from what may be called a *dynamic* standpoint. By these, developmental processes are looked upon as expressions of changes in equilibrium. Chemical and physico-chemical reactions are brought into play. The language of a chemist is exemplified in the contention that growth appears to be “the expression of autocatalytic chemical reaction,” and particular cycles of growth of an organism are accordingly shown to obey a precise mathematical formula. Somewhat more tangible than the distinctly hypothetical analyses of the chemical character of life phenomena and the physical structure of living matter are the conceptions of those scientists who aim to correlate growth with *nutrition*, emphasizing in some cases the material side and expressing the relationships in units of matter, or in others combining with

this the energy aspects and speaking in terms of calories. Lastly there are the considerations of the gross increase in size and form and other features, in which *statistical* factors assume the dominating importance. None of these aspects are without significance in the conception of growth; and if the biology of its processes still seems obscure, we must remember the complexity of the factors and forces which interplay in life.

What is growth? One cannot penetrate far into the literature of the subject without meeting with a bewildering confusion in the significance of the term. Various expressions, such as growth, organic growth, development, and euplasia have been applied to the same phenomena; and the numerous attempts to define their meaning and precise application have almost invariably ended in a failure to meet criticisms which might be urged against each definition submitted. The most general definition of growth is "increase in volume" or "increase in size" (Huxley). It has been pointed out, however, that increase in volume does not always serve as an index of organic growth; for the increase may merely be due to swelling. Sachs defined growth as an increase in volume accompanied by a change in form. Little is gained by defining growth as the result of a process of molecular intussusception (Huxley) or as due to excess of assimilation over disassimilation (Verworn). No universally acceptable definition has been framed; nor is it likely that one can consider all of the manifold features of growth in a single category. Some of the more familiar uses of the word growth are even more confusing than the so-called scientific definitions. Thus it is said that a tumor "grows," though the processes described may be quite unlike the growth of an organism. And in the "growth" of a hydrocephalus the analogy is stretched still further. What is needed today is less of theory and more of facts upon which to build a more substantial conception of growth and formulate its fixed characteristics in words.

The justification to dwell for a moment upon a review of the more adequate definitions proposed lies in the emphasis which this may throw upon some of the problems encompassed in the concept of growth. Lee has presented the analysis of growth in these words: "All growth, whether of the cells, the tissues, or the organs, is the result of no more than three processes, viz., multiplication of



cells, enlargement of cells, and deposition of intercellular substance, the first two being the most potent of all. Increase in the number of cells is largely, although not wholly, an embryonic phenomenon; increase in the size of cells and deposition of intercellular substance are especially important from the later embryonic period through the time of birth and up to the cessation of body-growth. The most obvious result of the growth of the cells, the tissues, and the organs, is growth or increase in size of the body."

If organisms are composed of both living matter and formed substance, it is evident that a growth may result from the increase of volume of either of these. This viewpoint is somewhat broader than that which governs the usual attitude of the physiologist. If body weight is taken as the measure of growth, it may be pronouncedly altered by deposition or removal of reserve materials, such as glycogen and fat, as well as by the retention of water and other products. In the narrower and stricter sense this is not growth. In many individuals the end of growth, as the physiologist intends to apply the term, is reached long before the gain in body weight ceases to manifest itself. Real growth in man, for example, usually is considered to stop at an age of 25 to 30 years when body length has reached its maximum. Many individuals continue to gain in weight and size until they are 50 years old; but this is of quite a different order than the gains in earlier years.

All of these considerations—cell division, increase in number or volume of cells, etc.—fail to take into consideration some of the most striking features of growth as it applies to the higher organisms. Perfect growth and development implies a far reaching correlation of the various parts of the body. An upset in this nicely balanced relationship is speedily recognized as an anomaly. Energy and matter are insufficient to explain the consummation and maintenance of a normal as contrasted with an abnormal composition of the cells. The specificity of growth is something marked, particularly when we contrast the normal with perverted growth. The regularity and characteristic individuality of the ontogenetic development seen in each species has found expression in the explicit definition by Schloss: "*So können wir das normale Wachstum eines jeden Organismus auffassen als artspezifische korrelative Vermehrung der Körpermasse in bestimmten Zeitabschnitten.*" The corre-

lation feature in respect to composition and form, the time relations, the anomalies and irregularities involved, are thus brought out. Here, as elsewhere in physiology, abnormalities have often given the clue to the understanding of normal processes.

Inasmuch as growth involves a more or less continuous change, there is need of some criterion thereof—some suitable method of ascertaining and measuring it. This is by no means as readily accomplished as might appear at first glance. Changes in body weight are not always reliable guides. There are increments of weight which are transitory and those which are permanent. Uncorrelated increments of mass may occur in the body long after the conclusion of what is properly termed the period of growth. A gain of weight at the middle life, for example, may be due to a deposition of reserve materials. Increase in stature and certain other dimensions are not without significance as indications of growth; for they allow us to estimate the correlation between weight and size. Without suitable proportionality of form perfect growth, to say the least, cannot go on.

How illusory the dependence on any one criterion of growth, such as body weight, may be is illustrated by the interesting studies of Waters and of Aron. These investigators have described conditions of adverse nutrition in young animals in which no change in body weight occurred during long periods of time. Nevertheless the animals "grew" from the standpoint of changes in stature and body proportions. In some cases the skeleton grew at the expense of other parts of the body, especially the flesh. Many of the organs retain their weight under such conditions, while the brain grows to reach its normal size.

Is the constancy of live weight an indication of lack of growth? If one allows the term "growth" for the phenomena of distortionate change here cited, it must be admitted with Aron that the "growth" depends principally on the tendency to grow possessed by the skeleton. Evidently, then, there are limitations to the dependence on weight measurements. They tell us nothing about the intricate changes in the tissues that may distinguish the adolescent from the adult form, nor do they serve as an index to the desired development of the body in three dimensions,—in other words of proportionate growth. Nevertheless the study of growth by weigh-

ing has hitherto furnished the best measure of the total changes of the body.

During growth the compounds and elements of the body are undergoing change and chemical variations. A detailed knowledge of what these are is desirable from many points of view. At the present day only the beginnings in this direction have been made. The work of obtaining statistics as to the varying chemical composition of the component parts of the growing organism at different periods of development involves laborious analyses, with the added difficulty that in order to secure data an experiment must be stopped by the sacrifice of the subject for examination. The correlation in development between different organs and tissues, the appropriate symmetry and interrelation of the parts, the changes in the "*körpergestaltende*" as well as the "*körpervermehrnde*" function are deserving of close investigation. The inroad into these and related fields has been begun.

When the statistics derived from periodic measurements of the continuous changes going on in young animals are expressed in graphic form, the so-called curves of growth are obtained. The fixity of the growth curve for the different species and, in so far as this point has been studied, of the sexes in each species is perhaps the most remarkable phenomenon of growth. "We are aware of no conditions compatible with life in which the general character of the growth curve with its acceleration during adolescence can be altered. Minor variations may, however, arise." Variations in the growth of different individuals are for the most part inborn—inherited fundamental characteristics of the individual. We know of no method or means of altering the peculiarities of growth. Nutrition, which is often looked upon as a controlling factor, can do no more than give free scope to the inherent tendency to grow. As Rubner has remarked, the hope of altering this tendency is quite as utopian as the attempt to prolong life indefinitely.

It has already been pointed out that the cells need not be the sole factors involved in the increase of size attending growth. Extracellular parts may come into play. Nevertheless the importance of the cells as the material basis of biological phenomena and the seat of physiological functions has tended to center attention upon these histological units in growth. We are brought face to face with the

question whether the size of an organism depends upon the size of its component parts—its cells,—or upon their number. Does an organism grow by increase in the number of new cells or by an enlargement of the old ones? In other words, is there a relation between body size and cell size? It would take us too far afield to examine in detail the evidence bearing on this and related morphological questions of the nature of growth. They have been vigorously debated. The answers probably differ for unlike species and certainly for different tissues. If in the lower forms of life differences in ultimate body size are due in the main to differences in cell number, the cell size being approximately constant, it by no means follows that this statement holds throughout the progressive stages of growth in higher organisms where other factors than cellular increase and enlargement also are involved. Perhaps we may distinguish between the processes of tissue differentiation and growth by reference to the changes in the number and the size of the cells respectively. Much has been made of the necessity of maintaining a certain proportion between the size of the nucleus and that of the cytoplasm composing the body of the cell. Doubtless physiological functions are closely associated with the presence of the nucleus and it appears that when a cell is to attain a very large size it is almost always found to contain several nuclei. Indeed, as we shall see, Minot has presented the relative increase in the cytoplasm with accompanying differentiation as the proximate cause of senescence.

Experience shows that there is a fairly definite upper limit in size which the individuals of any species rarely exceed. There are forms for which the variations may be very wide (as has already been pointed out); and it is reported that some of the lower forms, *e. g.*, actinians, can be caused by suitable feeding to reach a colossal size far beyond that which they ordinarily attain in nature. To the mammalian species with which we are primarily concerned here, however, this does not apply except in the limited degree determined by heredity. Why the body size is thus fixed is not known. The fact of its invariable character makes it possible to apply quantitative methods to the study of growth with some confidence in the consequences which are to be expected from any normal procedure, and with some appreciation of the standard to which proper growth should conform and by which all deviations are to be measured.



Quite aside from the question as to what initiates growth, the capacity to grow—the “Wachstumsfähigkeit,” “Wachstumsmöglichkeit” as it has variously been termed—is commonly made a property of the cells of the organism. Whatever may be the ultimate cause of growth, the capacity to grow is currently associated with a youthful character of the cells involved. From this standpoint age is an important factor in the possibility of growth. An embryonic condition of the cells is accordingly most favorable to growth. Minot’s third law of age, dealing with the growth function reads: “The rate of growth depends on the degree of senescence.” From a purely theoretical standpoint it is quite conceivable that ordinary cessation of growth may be due to a natural *inhibitory* factor which develops in the course of time rather than because the capacity to grow is lost. Nevertheless the idea that the growth power inevitably declines and is lost with age has found a firm foothold in physiological literature. The current notions may best be set forth by a few quotations. Donaldson has written that “the capacity for undergoing expansive change is transient, and that those cells which fail to react during the proper growing period of an animal have lost their opportunity for ever.” This has likewise repeatedly been urged by Rubner. We do not know in truth, he says, whether Nature demands an absolutely uniform daily growth, or whether remissions in growth are permitted or even advantageous. This alone is certain, that interference with the growth impulse should not last during the entire period for growth; otherwise the size of the individual will suffer permanent detriment. “Verlorene Körpergrösse in der Jugendzeit kann nach Vollendung der wachstumsperiode nimmermehr abgeglichen werden.”

In his entertaining book on *The Problem of Old Age, Growth and Death*, Minot has hinted that some factors other than nutrition and age may enter into the question here discussed. “When the cell is in the young state, it can grow rapidly; it can multiply freely; when it is in the old state it loses those capacities, and its growth and multiplication are correspondingly impeded, and if the organization is carried to an extreme, the growth and the multiplication of the cell cease altogether. We find, however, that there is something a little more complicated yet to be considered, for it is not merely a question of the capacity of the cells, but also of the exer-



cise of that capacity, which we must deal with. Here comes in a factor which we learn from the study of regeneration."

Experiments which have been conducted for some time by my colleague Dr. Thomas B. Osborne and myself, under the auspices of the Carnegie Institution of Washington, make us hesitate to accept some of the older dicta respecting the limitation of growth to a very definite period of life. We have secured clear evidence that the growth of rats and mice may be suppressed or held in abeyance for very long periods, even beyond the age at which any marked increment of size ordinarily occurs, without loss of the capacity of subsequent growth under appropriate conditions of diet. It is necessary to distinguish clearly between growth and regeneration or repair; for the latter is admittedly observed in the adult period of life.

The natural cessation of growth is a fact familiar to everyone. As growth proceeds and the powers of the individual mature, his tendency to grow rapidly declines. This is an interesting phenomenon that has not been explained. Minot in particular has promulgated the view that there is from a very early period a marked failing in the capacity to grow, due to factors in the animal body itself. The notion that senescence finds its beginning in the very earliest periods of life is not a new one. Thus, Thomas Cogan, author of *The Haven of Health*, writing in 1596, says: "And if we do consider well the state of mankind in this life, we may see that a man beginneth to die as soone as he is borne into this world, for that the radicall moisture which is the roote of life, can never be restored and made up againe, so good as it was at our nativitie, but continually by litle and litle decaieth untill the last end of our life. Yet by that moysture which commeth of nourishment, through meate and drinke, it is preserved and prolonged, so that it is not so soone wasted and consumed as otherwise it would be. Like as a lampe by powring oyle moderately, the light is long kept burning, yet it goeth out at the last. And this is it which Hippocrates speaketh: The same heat which brought us forth consumeth us. Yet in the beginning of our age while nature is yet strong, more of the nourishment is converted into the substance of the bodie, than is consumed: and that while the bodie increaseth and groweth. Afterward so much only is restored as is wasted, and then the bodie is in

perfect growth. At length nature waxing weaker, is not able to restore and repaire so much as is wasted and decayed, whereby the body beginneth to decrease, and the powers and strength thereof be more and more diminished until such time as life, even as the light of a lampe, be cleane extinguished. And this is called naturall death, which few attaine unto, but are prevented by death casuall, when by sicknesse or otherwise the said naturall moysture is overwhelmed and suffocate. Now the meanes to preserve this naturall moisture, & consequently to preserve life, is to use meates and drinckes according to the age of the person. For the dyet of youth is not convenient for old age, nor contrariwise."

According to Minot, the more rapid growth depends upon the youth of the individual—its small distance in time from its procreation. Cessation of growth is thus associated with age. We are told that there is "a certain impulse given at the time of impregnation which gradually fades out." The facts of regeneration in the lower forms warn us, however, to be cautious in drawing conclusions as to the loss of growth power. Something may *inhibit* it as age progresses. It has even been alleged that growth is stopped because an animal can digest only a limited quantity of food, and that the adult size is the stage of equilibrium between the amount of food digested and the amount used up. Experience in the field of nutrition speaks against such an assumption.

If we turn our attention to the unit of biological activity, the cell, in seeking something more specific respecting the decline or cessation of growth, certain general principles may be drawn into consideration. In a unicellular organism under favorable conditions of nutrition the process of building up exceeds the destructive process so that the body increases in size up to a limit where fission takes place. "What determines the limit is unknown, but the cause is perhaps in some way connected with the geometric principle that the volume of the cell increases as the cube of its diameter, whereas the surface by which it absorbs nutriment and otherwise comes into relations with the outside world increases only as the square of its diameter." Since activity is a function of the surface the larger the unit the smaller must be its activity. An organism can only attain a large size on this basis, by a multiplication of units, each presenting the same amount of surface as an individual cellular organism,

though it may be exposed to an internal rather than an external medium. One of the secrets of the cessation of growth in higher forms lies in the limitation of this cell division.

A further aspect of the cessation of growth concerns the relations of nucleus to cytoplasm in the growing cellular masses. The functions of nutrition and growth in cells depend upon the presence of a nucleus. Cells which attain a very large size may contain many nuclei. The process of cell division is determined by the ratio of the mass of nuclear chromatin material to that of the protoplasm of the cell. Jacques Loeb has pointed out that after fertilization there is an enormous synthesis of nuclear material. He suggests the possibility that the ratio determining cell division may be determined by the laws of mass action and chemical equilibrium. This synthesis of nuclear compounds from the protoplasmic constituents is a reversible process, according to Loeb. If there are continual readjustments to dispel the disproportion between nuclear and protoplasmic material, the cessation of growth may be correlated in some way with the final establishment of equilibrium according to definite chemical laws.

Abnormalities of growth are attributable to manifold and diverse causes. Constitutional defects, faulty nutrition, and various environmental factors may be more or less responsible. It is correspondingly difficult to classify on an etiological basis the manifestations which they occasion. There occur deviations which are presumably still within the realm of the normal. This applies, for example, to the variations in the growth of the individuals of a litter, or between different litters. Anomalies of growth expressed by an *exaggerated rate* are among the rarities of physiology. Instances of early gigantism which might fit this category have been described. The more frequent cases of rapid growth usually represent recovery or response to suppressed growth rather than actual growth *de novo*. In other words, whenever the growth of an entire organism as well as that of individual organs is modified in the sense of acceleration this usually involves the reversal or return of a morbid condition to the normal.

Inhibitory features of growth may manifest themselves by abnormally diminished growth, untimely complete cessation of growth (Wachstumsstillstand), or even decrease in size. Defects of nutri-

tion are a common cause of slow growth; but even with adequate diet there may arise a condition of maintenance without growth. Here we enter the realm of dwarfed or stunted individuals. The complete suppression of growth has been accomplished by Osborne and myself in a variety of ways which are not primarily attributable to underfeeding. The energy factor, as such, thus drops out of the problem. In this respect the experiments are not comparable with those of Waters and of Aron, both of whom accomplished their results by underfeeding with adequate food materials. In our experiments the "energy requirement for maintenance" and the "energy requirement for growth," which together are essential to the developing organism, were both supplied. Our dwarfed rats did not grow primarily at the expense of stored tissue materials: in respect to gross form they apparently failed to grow in any sense. If it is true that growth can only continue when the energy intake exceeds the mere maintenance requirement, it is equally true that an excess of calories does not *per se* insure growth in a suitable animal. This fact furnishes an opportunity to the investigator to ascertain and differentiate some of the essential qualitative factors: protein, inorganic salts, etc.—their minimum and optimum values.

Progressive decline in weight, negative growth (kataplasia), is an obviously pathological manifestation. Like most of the abnormalities of the adolescent period its clinical manifestations are of decided importance.

Irregularities of growth in the individual tend to be followed by compensating processes. Statistical studies on children, for instance, indicate that retardation in early growth is made up by abnormally rapid growth later. Whether all growth really stops in such instances, or whether our measurements do not merely indicate a loss of special body substances such as stored nutrients, needs to be determined. The answer has a bearing on the question already raised whether in the recovery process we are really dealing with new growth or with restitution of depleted tissues.

Attempts to influence growth by drugs, such as alcohol, nicotine, caffeine, etc., are recorded in the literature. They need not be detailed in this connection. It should be remembered that the obvious effects are not the only ones which may enter into the pathology of



growth; defects may occur unrevealed in the curves or gross manifestations, yet involve the finer structures of the organism which are hidden to the naked eye.

The use of the term growth with its several connotations has not infrequently led to a confusion with phenomena which are in reality distinct therefrom. The distinctions are frequently subtle, yet none the less important. Thus the pathologist employs the terms hypertrophy and hyperplasia, the latter type of enlargement being the one dependent on the formation of new cells. In mammals, for example, there is no hyperplastic growth in the nervous elements after birth. Other tissues, such as the connective and epithelial varieties, show abundant hyperplasia.

The increase in size or weight that is observed in *adult* life has also been correlated with growth. The processes are presumably distinct. This addition to the organism or deposition of new material therein—the “Körperansatz” or “Mast” of the Germans—plays an important part in the “finishing” of cattle for the market. The “Ansatz” may be of a more permanent type such as characterizes the deposition of fat, glycogen or even protein in the cells; or it may be decidedly “unstable,” representing water largely rather than food elements assimilated in proper proportions. This latter aspect of the storage depots in the body, in which water is present in exaggerated amounts, is not infrequently met with in pathology. True “Ansatz” must be distinguished, furthermore, from repair (reparation, realimentation, reconvalescence, recuperation, recovery) which takes place when by inanition, disease, or malnutrition, or all combined, growth has been checked in the adolescent or body weight lost in the adult. The increase in size attending realimentation has not infrequently been confused with true growth. They may be, and presumably are, distinct processes. In the one case depleted structures are restored, in part by mere deposition and restitution of the storage depots; in growth, novel changes are initiated in addition. There are indications available that the chemical and metabolic processes of repair are by no means identical with those of growth.

Growth and regeneration undoubtedly have much in common; yet they deserve individual treatment. Quoting Morgan, “the word ‘regeneration’ has come to mean, in general usage, not only



the replacement of a lost part, but also the development of a new whole organism, or even a part of an organism, from a piece of an adult, or of an embryo, or of an egg. We must include also those cases in which the part replaced is less than the part removed, or even different in kind. . . . The term 'physiological regeneration' I shall use in the ordinary sense to include such changes as the moulting and replacement of feathers, etc.—changes that are closely related to the life cycle of the individual." The power of regeneration in the general sense diminishes as we ascend the vertebrate scale. Morgan believes that at least one reason for this lies in the lack of coördinate regeneration in the higher vertebrates, *i. e.*, the slowness of certain tissues to regenerate in time with the other tissues. Inasmuch as this has an indirect bearing upon the possible causes of the uncorrelated growth which manifests itself as a pathological phenomenon at times, it may be worth while to quote Morgan's view in some detail. He writes: "The evidence indicates, I think, with some probability, that the failure is due to the fact that the different tissues have very different rates of regeneration. In other words, each tissue in man seems to possess the power to regenerate its kind, but not all at the same pace, hence they fail to coöperate at the proper time to form a new structure. In man the skin regenerates; the muscles regenerate, though less well, perhaps; the nerves and the blood vessels regenerate, and the bones even have a not inconsiderable power to mend and even to some extent to regenerate. Hence, as I have said, the failure of the new limb to develop does not appear to be due to the failure of the individual elements to regenerate, but is due to their failure to regenerate concurrently. The bones or the nerves or the muscles may be the main cause of the trouble, for they produce new material with great slowness."

The entire field of the physiology of repair is largely unexplored as yet. Losses due to simple inanition can apparently speedily be made good. Whether the end result as regards the composition of the restored tissues is the same as that pertaining in normal growth remains to be seen. If it is true that the capacity for regeneration implies a latent youthfulness the extent to which loss in weight is compatible with continuation of life may in part be dependent on the latent power of growth as well as repair. Practically this finds

its expression in conclusions such as that the younger the child the more readily is recuperation accomplished. It appears to be a fact of experience that animals retarded in growth by underfeeding, as well as young children recovering from prolonged illness, begin to grow with more than normal vigor on a return to normal diet and health conditions and at the end of the growing period may be as heavy and have as heavy a brain as their normal companions. Nevertheless this will not yet justify us in concluding that the restored individuals are in all respects normal. Qualitative changes not appreciated by the cursory examinations may have become permanently engrafted.

In all of the foregoing discussion of the phenomena of growth, its varied aspects, the criteria, the modifying factors and related phenomena, little has been said of the initiation of this fundamental manifestation of living organisms. What is the underlying cause of growth? Like other biological processes this one can as yet be defined satisfactorily only in terms of its manifestations. The cause of regeneration is loss of body substance. It may frankly be admitted at the outset that we know almost nothing in regard to what takes place in protoplasm during growth and very little regarding the causes which incite or inhibit it. The only justification for veiling this ignorance in a vague terminology lies in the help which formulated hypothesis often brings to the solution of obscure problems. With this prefatory statement growth may be defined as the resultant of an inherent growth impulse—an internal factor—and a suitable environment, the latter including the food supply—an external factor. In these are concerned certain typical biological forces, the metabolism of matter and energy, as well as certain physio-chemical reactions. The conditions determining growth are mainly resident in the cells.

If we are unable today to define the internal factor suitably, it is equally impossible to cite all the external factors as we do for plants. Air, light, warmth, food, etc., have their functions. However essential food may be for growth—and no one can gainsay its preëminent importance—it can in no sense be regarded as the supreme *cause* of growth. Nutrition can only give the growth impulse free play. This factor can, however, be subjected to experimental analysis. The rôle of the individual nutrients,—organic and

inorganic,—the energy features and other nutritional details can be studied with some precision. But of what we have called the *internal* factor in growth—the growth impulse, the tendency to grow, the capacity to grow, “Wachstumstrieb,” “Wachstumsfähigkeit,” “Wachstumsmöglichkeit,”—the factor which is hereditary in its origin and sets to growth the limits which nutrition cannot fundamentally alter, little further can be said. It may be that the rhythm of cell division and its attendant features, which some have identified as the detectable expression of the capacity to grow, is dependent upon the action of “hormones,” products of internal secretion and cellular metabolism. If this is true we shall have at our disposal some means of modifying the internal factors of growth. For the present we must content ourselves with the unsatisfying conclusion that to unravel the inner nature of growth is to penetrate the secret of the distinguishing characteristics of living substance. Here hypotheses reign uncontrolled.

However dominant the rôle of the cell in growth may be, the problem of development cannot be investigated solely from the standpoint of cellular physiology. We may admit the limitations of nutrition in furnishing an adequate explanation of either the “Wachstumstrieb” or the “Wachstumsmöglichkeiten”; but in any event the food factor in growth is one that is open to experimental study. The greatest hope of advance in the solution of the obscure questions of growth therefore appears to lie in this direction.

Along this direction, for example, Osborne and I have found with our coworkers that not all proteins suffice to promote growth. Some of them are apparently adequate to fulfill the needs of both maintenance and growth; others like gliadin satisfy the requirement of maintenance alone; while such “incomplete” proteins as zein and gelatin are by themselves inadequate in every sense for perfect nutrition. The incapacity of some of these proteins unquestionably lies in a lack of certain essential amino-acid units. It must be noted that growth has not been accomplished with any protein lacking the cyclic groups such as are found in tyrosine, phenylalanine, and tryptophane; and we have lately found that lysine is indispensable for tissue construction. That these “inefficient” proteins are not primarily toxic to the organism is shown by the fact that we have found many of them to be adequate for maintenance in both grow-

ing and adult organisms; whereas, as is well known, others like zein and gelatin by themselves do not even suffice for this function. The need of an adequate supply of energy in some form or other, and of appropriate salts for tissue construction is obvious. The importance of the latter gains an unsuspected prominence when one plans experiments with isolated food substances; for with the ordinary natural food mixtures a reasonable modicum is already provided. We are convinced from an extensive experience that many failures to promote growth in experiments on artificial nutrition have centered in the inorganic food ingredient of the selected dietaries. In some instances the deficiencies, if such there are, may involve some minute proportion of hitherto supposedly inessential elements like iodine, manganese, etc. The time and opportunity for investigation along the lines here suggested has arrived. There is, further, a considerable body of evidence to suggest that "hormones" or "vitamines" or comparable stimulants of growth are essential. It is futile as yet to discuss their mode of action. In any event, however, their rôle among the external causes of growth need not be that of a simple nutrient in the sense of yielding energy or material for development.

The analysis of growth into a controllable nutrition factor and an inherent growth impulse has its significance for the appreciation of the pathology of growth and the management of the situations created thereby. It becomes clear that abnormal growth cannot always be corrected by regulation of the external factors of diet, etc. A limit to dietotherapy or other therapeutic measures is oftentimes set by the inalterable inheritance of an imperfect constitution, the basis of an adequate capacity to grow.

To attempt to formulate "laws" from data which are not overabundant and which involve a considerable number of variables can scarcely be expected to yield generalizations of a very exact nature. Nevertheless there have been essays at probable laws for growth. As an illustration I may cite Lusk's generalization that "during the normal development of the young of the same age and species, a definite percentage of the food is retained for growth irrespective of the size of the individual." Rubner has independently applied a quite similar law to the growth of all species except man, as an expression of the belief that it requires the same energy



equivalent to construct a unit of new substance in young animals. Rubner has also formulated conclusions regarding the length of life of individual species in relation to the number of calories metabolized during life. Exact mathematical expressions have already been devised for certain features of growth. In the light of our scattered knowledge I can only agree with Friedenthal that in biology it is best to avoid the term "law" and content ourselves with generalizations which have their exceptions and are not absolute in their comprehension. We are still far from the stage where laws of growth can successfully be propounded. The path which the natural sciences have successfully pursued in the past has not led from proposed laws to facts, but rather in the reverse direction from the collection of facts to generalized rules. This is likewise the way which the research of the future must follow.

It is almost impossible to review the salient features of the physiology of growth without directing attention to the obvious gaps in our knowledge thereof. Problems await us at every turn,—some of them clearly defined and open to experimental investigation, others obscured in the haze of conflicting data or complicated by the manifold factors which enter into the questions of development. No review of any aspects of a progressive and growing science is complete or illuminating unless it suggests problems as well as answers them. A passing reference to some of them may not be inappropriate here. Statistics of growth being the easiest to obtain, have been collected in greatest number. But there are numerous statistical details involving the growth of the individual parts or organs which are quite as essential for the understanding of what is involved in the correlation between organs incidental to growth.

More than ever the need of additional studies of the histology of growing tissues in mammals looms up at the present time. They are fundamental to any investigation of the morphological background against which the growth functions are projected. The popularity which histological investigation has enjoyed in embryology in recent years should be extended into the postnatal stages of life. In general we are taught that different tissues have unlike power of growth in the sense of cell multiplication. Some, like the testes, multiply their cells throughout life; others, like the muscles



and nervous system, only in the embryonic period; others again, like the glands, during a variable period after birth. So long as so much emphasis is placed upon the cell in growth we deserve to know more about its morphological history in this crucial period; and this applies above all to those tissues, the so-called ductless glands, like the hypophysis and thymus which it is currently customary to associate in some way with growth. Until very recently the interest of histologists has centered either in the embryonic or the adult tissues of mammals, with scanty consideration of the intervening stages.

The importance of a comprehensive consideration of nutrition in growth need not be dwelt upon in detail. The conflicting views which have been held since Liebig's time regarding the significance of protein in nutrition have had their counterpart in the explanation of growth. Voit assumed that the protein metabolism of the growing organism is unlike that of the adult. The inadequacy of the theories which associate growth with a decreased power of protein katabolism no longer requires emphasis. Now that we know of the marked chemical and biological differences existing between proteins from different sources the significance of these facts in nutrition must be further established.

Important economic considerations are involved in the ability to modify growth or accomplish it at lessened expense,—a possibility for which nutritive factors offer the only probable opportunity at present. Hence arises the practical importance of some of the problems in this field. Broadly put, one problem reads: How can inefficient native foods be made efficient, and what is the relative economy of different dietaries and adjuvants?

The questions which arise in connection with the duration of the capacity to grow have already been alluded to. Will growth, suppressed by the necessary restrictions in diet, cease entirely for an indefinite length of time? What happens to an animal suffering such a suspension of growth, when it is given an abundant diet? What are the tissue changes accompanying these suppressions and realimentations, *i. e.*, what are the attendant histological features?

The function of age is evidently an important matter for consideration in questions of growth. An index of age apart from the record of birth is much to be desired. Weight and size in general may be inadequate for many obvious reasons. What can be

accomplished in this direction is indicated by the investigations of Donaldson and Hatai on rats. They have found that the percentage of water in the central nervous system is a function of age and under ordinary conditions, whether the animal be over size or under size, well nourished or ill nourished, with a large brain or a small brain, the percentage of water remains practically unmodified by these conditions. The deviations in extreme malnutrition even are, very slight at most and completely disappear on a return of normal nutritive conditions. The percentage of water in the central nervous system accordingly is the best index yet available of the normal process of senescence. The facts fit in with human experience in showing that hardships which include underfeeding need not necessarily shorten the span of life. It is no small advantage to have a dependable index of age. The experimental possibilities and desiderata in this field are far from exhausted. Chemical data are needed to supplement the histological and other analyses of age.

Although each individual appears to strive to attain a definite size it is still debated whether nature demands continuous growth or to what extent remissions are detrimental or permissible. It is becoming more and more evident that growth is not an entirely indispensable function of living matter. Otherwise stated, the failure to grow is not incompatible with life. Where are the limitations of such situations? And above all, can life be extended by the delay of growth? This is one aspect of the broad problem of prolonging life artificially by altering the conditions under which it goes on. Theoretically it is conceivable that growth processes, like chemical reactions, should be reversible.

The more detailed study of growth may be expected in the future to bring helpful experience to bear on the manifestation of pathological neoplasms which concern health so vitally. The competition of youthful cells such as those of malignant tumors with the normal cells of adult tissues frequently brings victory to the younger tissue. The problems of normal development and abnormal structure are doubtless in many respects one and the same.

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“Every great advance of science opens our eyes to facts which we had failed before to observe, and makes new demands on our

powers of interpretation. . . . Great as the advance of scientific knowledge has been, it has not been greater than the growth of the material to be dealt with. The goal of science is clear—it is nothing short of the complete interpretation of the universe. But the goal is an ideal one—it marks the direction in which we move and strive, but never a stage we shall actually reach. The universe grows ever larger as we learn to understand more of our own corner of it.”

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## THE PHYSICO-CHEMICAL BASIS OF STRIATED MUSCLE CONTRACTION

### 3. The maximum surface tension in striated muscle

WILLIAM N. BERG

#### INTRODUCTION

About a year ago, the writer<sup>1</sup> published some calculations on the lifting power of striated muscle, in which an attempt was made to ascertain whether the changes in the surface tension between the contractil units and their surrounding medium were great enough to account for the lifting power of striated muscle.

Among others, the assumption was then made that at the moment when a striated muscle begins to contract against an external resistance, the surface tension between the contractil units and their surrounding medium (presumably the sarkoplasm) might possibly be as high as 85 dynes per cm. This was regarded as the upper limit, altho certain data in the literature, to be presented later, plainly indicated that the upper limit could not be so high. Several assumptions were made in favor of the surface-tension theory for the purpose of justifying the temporary or provisional use of 85 dynes per cm. as the maximum surface tension between the contractil units and sarkoplasm. A minimal surface tension was likewise assumed from the literature for the relaxation phase, but as this figure was purposely and provisionally omitted from the final calculations, it may be disregarded for the present.

The results indicated that in a working striated muscle, surface energy can furnish but a small part of the total energy transformed, a conclusion diametrically opposed to that of Bernstein, Macallum<sup>2</sup> and others, who regard a working muscle as a mechanism that can transform a quantity of surface energy equivalent to the external work done.

<sup>1</sup> Berg: *BIOCHEMICAL BULLETIN*, 1912, ii, p. 101.

<sup>2</sup> Macallum: *Jour. Biol. Chem.*, 1913, xiv, p. 96.

As further evidence of the correctness of the surface-tension theory, Macallum<sup>3</sup> recently quoted Jensen<sup>4</sup> to the effect that "a thread measuring one mm. in diameter formed of the plasmodium of *Chondrioderma*, a *Myxomycete*, may, when it is in the dense condition, bear up a weight of nearly a gram. If the force engaged is surface tension it would amount to about 6000 dynes per cm." Because of its enormity this figure of Jensen's at once arrests the attention, for nowhere in the annals of physics and chemistry, can a surface tension of 6000 dynes per cm. be found. Most organic substances that are fluid at ordinary temperatures, have surface tensions well below 50 dynes,<sup>5</sup> when measured against air. Very few aqueous solutions have surface tensions higher than 85 dynes per cm. For a large number of molten salts the figures vary between 100 and 200 dynes. For most of the metals, when melted, the figure varies between 250 and 1000, altho platinum seems to be exceptionally high, having a surface tension in the molten state of about 2000 dynes per cm.<sup>6</sup>

Presumably, the plasmodium of *Chondrioderma* has a chemical composition similar to that of other living matter and consists essentially of water plus the usual materials present in living matter. The surface tension of water, when measured against air at ordinary room temperatures, is about 70 dynes per cm.<sup>7</sup> Altho small amounts of some organic substances can lower the surface tension of water considerably, the surface tension of water cannot be raised very much by any substance, even when present in large amount. There seems to be an upper limit to the surface tension of aqueous solutions (in exceptional cases this is as high as 109 dynes per cm.

<sup>3</sup> Macallum: *Jour. Biol. Chem.*, p. 110.

<sup>4</sup> Jensen: *Anatomische Hefte*, 1905, xxvii, p. 842.

<sup>5</sup> If not otherwise indicated, figures for surface tension are in dynes per centimeter, i. e.,  $\frac{\text{dynes}}{\text{cm.}}$ . The magnitude of the dyne can be easily grasped if it be borne in mind that a mass of 1 gram is attracted to the earth with a force of 1 gram, or 981 dynes. Consequently, a dyne is practically equal to a milligram (force).

<sup>6</sup> Freundlich: *Kapillarchemie*, pp. 30, 62 (Leipzig, 1909). Landolt-Börnstein: *Physikalisch-chemische Tabellen*, 4te Aufl., pp. 114-129 (Berlin, 1912).

<sup>7</sup> Landolt-Börnstein: *Loc. cit.*, pp. 112, 128, 129; Freundlich: *Loc. cit.*, p. 62; Lewis: *Ztschr. f. physikal. Chem.*, 1910, lxxiv, p. 619; Heydweiler: *Ann. Physik.*, 1910, xxxiii, pp. 145-185.



for very concentrated solutions of potassium carbonate), which varies from 71 to 85 dynes per cm. for the aqueous solutions of most inorganic salts. From the data in the literature, one might infer that the surface tension of Chondrioderma ought not exceed that of other aqueous solutions or suspensions of comparable composition. It should, therefore, be somewhere in the neighborhood of 85 dynes per cm., or below. But according to Jensen's calculations, it is 6000 dynes per cm.. One reason for doubting the correctness of this figure has already been mentioned, namely, the fact that surface tensions as high as this are not to be found recorded in the literature, for any substance. Secondly, Jensen apparently overlooked the fact that the circumference of a circle is  $2\pi$  times the radius and not  $\pi$  times the radius, which is the expression used in Jensen's<sup>8</sup> formula, with the result that a quotient of 6000 ought to be 3000.

A somewhat similar error was made in our own calculations already published,<sup>9</sup> insofar as the value of  $\pi$  was accidentally omitted from the value for the reduction in area when 1 cc. of muscle contracts. The value previously obtained, 1000 sq. cm., should be a little over 3000 sq. cm., with corresponding changes in the results. So many assumptions had been made in favor of the surface tension theory, that no change was necessary in the final conclusion, namely, that the surface-tension theory of striated muscle contraction as advanced by Bernstein, by Macallum and others, is untenable. It is rather remarkable that altho Bernstein's<sup>10</sup> calculations showed that surface energy was insufficient (p. 295), and he realized the insufficiency, he still advocated the theory as being correct in principle (p. 141).

<sup>8</sup> Jensen, *loc. cit.*, p. 841: "Diese (the surface tension) ist berechnet aus dem Gewicht, das ein Pseudopodienbündel von bekanntem Gesamtumfang zu heben vermag. Die Berechnung geschah nach der Formel  $a = p/\pi r$ , wo  $a$  die Oberflächenspannung,  $p$  die Zugfestigkeit eines Pseudopodiums und  $r$  sein Radius ist." Jensen used this same formula in the two widely differing cases of a thread (Orbitolites) that lifts a weight and a thread (Chondrioderma) that sustains a weight. This is the probable reason for the great difference between the surface tensions of Orbitolites and Chondrioderma and not as proposed by Macallum (*loc. cit.*, p. 111): "It is not improbable, therefore, that surface tension may be very high in some forms of living matter and very low in others . . ."

<sup>9</sup> Berg: BIOCHEMICAL BULLETIN, 1912, ii, pp. 107-109.

<sup>10</sup> Bernstein: *Arch. f. d. gesammte Physiologie*, 1901, lxxv, pp. 271-312; 1909, cxxviii, pp. 136-141.

Jensen's arithmetically correct figure of 3000 dynes per cm. is still so very much higher than that of any known substance that one is led to suppose that perhaps Jensen's method of calculating the surface tension is incorrect. According to his formula, the weight sustained by a plasmodium thread when divided by the circumference of the thread gives the surface tension. This method may be correct, but it is not mentioned among the various methods described in the literature. This makes it desirable that someone prove its correctness.

To the writer it seems that the quotient obtained by Jensen does not represent a surface tension.

According to Pfeffer,<sup>11</sup> the question of surface tension does not enter the problem (of Chondrioderma) at all, for the reason that the outer layers of the plasmodium thread of Chondrioderma are solid at the time when a weight can be sustained. Or, to be more precise, Pfeffer states that Chondrioderma have the property of reversibly varying the consistence of the outer layer, from that of the fluid protoplasm in the interior of the cell to that of solid gelatinous masses. The tougher outer layer is regarded by Pfeffer as a physiological product, and not until this has been brought back to its originally fluid condition can changes in surface tension be regarded as factors in the problem.

If Jensen's formula gives results that have a real physical meaning, it ought to be possible to apply it to other forms of living matter and to obtain results that can be interpreted. Parnas<sup>12</sup> found that the smooth muscles of certain clams could sustain very great weights. He so loaded living, intact clams, that in one case (p. 458) a smooth muscle having a cross section of 0.3 sq. cm. sustained a weight of 3000 grams for three hours. Similar observations on the great weight-sustaining power of smooth muscle have been made by others.<sup>13</sup>

Assuming that the cross section was of uniform tensile resistance, each sq. mm. sustained a weight of 100 grams, which is 75

<sup>11</sup> Pfeffer: *Pflanzenphysiologie*, 2te Aufl. (1904), pp. 716-718.

<sup>12</sup> Parnas: *Arch. f. d. gesammte Physiol.*, 1910, cxxxiv, pp. 441-495.

<sup>13</sup> Bethe: *Arch. f. d. gesammte Physiol.*, 1911, cxlii, pp. 291-336. Cohnheim and von Uexkull: *Ztschr. f. physiol. Chem.*, 1912, lxxvi, pp. 314-321; Cohnheim: *ibid.*, pp. 298-313.

times the weight sustained by the 1 mm. thick plasmodium of Chondrioderma according to Jensen's observation, and which is quoted by Macallum as an example of high surface tension in living matter. Since a thread of this smooth muscle 1 mm. in diameter can sustain 75 grams, the surface tension between it and its surrounding medium, water in this case, must be over 468,000 dynes per cm. according to Jensen's formula. This value becomes 234,000 dynes per cm. if Jensen's formula be used as it probably was intended to be used (see p. 179). The correctness of such a figure and of the method used in obtaining it are to be doubted because the surface tension calculated in this way is greater than that of any other known substance.

The problem of the transformation of energy in striated muscle is, in part at least, a problem in dynamic mechanics. It seems strange that certain investigators<sup>14</sup> should attempt to treat the subject as if it were a problem in static mechanics. The plasmodium of Chondrioderma did not lift a gram, it did no work, for the weight was only sustained, and in this respect the phenomenon is comparable with the sustaining of very much greater weights by smooth muscle, but is not comparable with the lifting of weights by striated muscle. That the plasmodium could sustain a weight because of the surface tension between its surface and the surrounding medium is for the present purely an assumption, for neither Jensen nor Macallum have brought forward any evidence showing that surface tension was a factor in the problem.

#### THE SURFACE TENSION BETWEEN CONTRACTIL UNIT AND SURROUNDING MEDIUM

To know the limiting values of the surface tension between the contractil units and the surrounding medium is obviously of the greatest importance in connection with the surface-tension theory. Fortunately, the data in the literature on the surface tension between two liquids or between two solutions are sufficiently complete to point definitely to the limiting values desired. Two solutions are to be considered: (1) The solution of biological substances which constitutes the lateral surface of the contractil units and (2)

<sup>14</sup> Bernstein: *Arch. f. d. gesammte Physiol.*, 1901, lxxxv, pp. 271-312. Jensen: *Anatomische Hefte*, 1905, xxvii, p. 842.

the solution of biological substances which bathes these contractil units, and which probably is tissue lymph. It is assumed of course, that the transformation of energy into external work takes place on the lateral surfaces of the contractil units and not on their upper and lower bases (otherwise a muscle would be stronger crosswise than it is lengthwise).

These two solutions are assumed to be in contact with one another thruout the contraction and relaxation phases and, presumably, the surface tension between these two media is due to the *rapid chemical changes taking place both inside and outside the contractil unit*.<sup>15</sup> Insofar as the surface tension varies, being high just as contraction begins and being low (?) as relaxation begins, the chemical composition of the two solutions must vary continually, even when the muscle is apparently at rest, for then the condition of tonus still requires the expenditure of energy, tho in smaller amount.

How high can the surface tension be between contractil unit and lymph? It obviously cannot be higher than that of a saturated aqueous solution of the salts found in living tissue. In general, the organic constituents of lymph and of blood serum tend to lower the surface tension of water, the inorganic constituents tend to raise it. The effects of the former predominate in blood serum. Morgan and Woodward,<sup>16</sup> using very accurate methods, determined that the surface tensions of the blood sera of several kinds of animals, including man, were practically the same and that, at 37° C., it varied between 44 and 48 dynes per cm., when measured against air. That is to say, under ordinary conditions the surface tension of blood serum is two thirds that of water, both surface tensions being measured against air. Insofar as lymph and blood serum do not differ much in their composition, the above figure gives at least an idea of the value about which the surface tension in working muscle fluctuates. But the solution on the contractil unit may differ in its composition, for very short periods of time, from that of the surrounding lymph and it may have a higher surface tension.

<sup>15</sup> Berg: *Arch. f. d. gesammte Physiol.*, 1912, cxlix, p. 205.

<sup>16</sup> Morgan and Woodward: *Jour. Amer. Chem. Soc.*, 1913, xxxv, pp. 1249-1262. For further data on the surface tensions of serum, lymph, etc., see Neuberger: *Der Harn sowie die übrigen Ausscheidungen und Körperflüssigkeiten*, ii, p. 1724 (Berlin, 1911).



The surface tension may be raised by at least two processes: (1) Substances that lower the surface tension of water are removed, thereby bringing the surface tension up to that of water, and (2) inorganic salts are at the same time brought into the solution, thereby raising it beyond that of pure water. For the present it may be *assumed* that, at the beginning of the contraction, the contractil unit is covered with a layer of saturated sodium chlorid solution, because sodium chlorid is the most abundant inorganic salt present, and its saturated aqueous solution has as high a surface tension against air, *i. e.*, about 85 dynes per cm., as that of any other solution of biological substances. Concentrated solutions of sodium hydroxid and of potassium carbonate<sup>17</sup> are exceptional insofar as their surface tensions are somewhat higher than that of saturated sodium chlorid solution. These may be disregarded because of their absence from living matter.

It is altogether possible, and in fact quite probable, that the changes just described do not take place on the contractil unit. It should be borne in mind that the object of considering a saturated sodium chlorid solution as covering the contractil unit just before contraction is solely for the purpose of justifying the provisional use of the highest surface tension recorded in the literature for the aqueous solutions of biological substances. Eighty-five dynes per cm. is not a postulated value for the surface tension of the solution on the contractil unit at any time. What the actual highest value really is, may, for the present, be regarded as an unknown quantity. Eighty-five dynes per cm. is an *upper limit* for all the solutions in the active muscle—in which solutions the chemical and physical changes take place that presumably underlie the vital activities of striated muscle.<sup>18</sup>

Eighty-five dynes per cm. is the surface tension of saturated sodium chlorid solution against air at 18° C. What is the surface tension of saturated sodium chlorid solution against lymph? Presumably, the surface of the contractil unit is at all times in contact with another liquid, the lymph, and not with a gas. In the calcula-

<sup>17</sup> Landolt-Börnstein: *Physikalisch-chemische Tabellen*, 4te Aufl., p. 129 (Berlin, 1912).

<sup>18</sup> Freundlich: *Kapillarchemie*, p. 62 (Leipzig, 1909). Landolt-Börnstein: *Physikalisch-chemische Tabellen*, 4te Aufl., p. 129 (Berlin, 1912).



tions previously published<sup>19</sup> the assumption was made, in order to give the surface-tension theory the widest latitude, that the surface tension of the contractil solution (*i. e.*, the solution on the lateral surfaces of the contractil unit) against lymph is the same as it is against air, or in other words that the surface tension of lymph against air is zero. But this, of course, is not true. Lymph has a surface tension not very different from that of serum.

The theoretical maximum effective surface tension between the contractil solution and the immediately adjacent layer of lymph can be ascertained from (1) the maximum surface tension of the contractil solution against air; (2) the minimum surface tension of the adjacent lymph against air, and (3) the assumption that these two occur simultaneously at the beginning of the contraction phase. The second value subtracted from the first gives the figure desired. The surface tension between two liquids is equal to, or is less than, the difference between their surface tensions when measured separately against air,<sup>20</sup> provided they do not react chemically. For reasons already mentioned, the maximum surface tension of the contractil solution, against air, has been assumed to be 85 dynes per cm., or a value very close to it. In a similar way, the lower limit for the surface tension of the adjacent lymph, when measured against air, may be assumed to be the *lowest* surface tension recorded in the literature for aqueous solutions of biological substances.<sup>21</sup> A dilute solution of sodium oleate, or a concentrated solution of a fatty (butyric) acid,<sup>22</sup> both have very low surface tensions, very near 26 dynes per cm. Either of these solutions may be assumed to constitute the adjacent lymph at the moment when the contractil solution has its maximum surface tension. The surface tension between the contractil solution and the adjacent lymph, assuming that there is such a surface tension, would be the differ-

<sup>19</sup> Berg: *BIOCHEMICAL BULLETIN*, 1912, ii, p. 107.

<sup>20</sup> Quincke: *Annalen der Physik und Chemie* (Poggendorff's *Annalen*), 1870, cxxxix, pp. 1-89; Whatmough; *Ztschr. f. physikal. Chem.*, 1901, xxxix, p. 175; Antonow: *Jour. de chimie physique*, 1907, v, p. 372.

<sup>21</sup> An alternate assumption is possible: that the adjacent lymph is momentarily separated from the contractil solution by a layer of pure organic substance having a very low surface tension, *i. e.*, butyric acid, 26, or acetic acid, 23, dynes per cm.

<sup>22</sup> Freundlich: *Kapillarchemie*, pp. 56, 59 (Leipzig, 1909).

ence between the surface tensions of these solutions measured separately against air, *i. e.*, 85 minus 26 or very nearly a maximum of 60 dynes per cm.

What is the surface tension between contractil solution and adjacent lymph at the beginning of the relaxation phase? The most expedient answer is, zero; a condition which can arise when contractil solution and adjacent lymph have acquired the same composition, altho in certain cases (see p. 190) the surface tension may be zero between two solutions differing in their composition. The muscle relaxes presumably because its own weight is sufficient to reform the contractil surfaces against zero surface tension. This assumption taxes the theory least. If the surface tension during the relaxation phase is anything other than zero a second problem arises which is as great as the first, namely, to explain how a relaxing muscle, presumably doing no work, can, in the act of relaxation, re-form the large contractil area against a surface tension greater than zero. Naturally, the greater the surface tension at the beginning of the relaxation phase, the more work must be done in reforming the contractil area against the surface tension.

To summarize: In order that there may be a surface tension between the contractil solution and the adjacent lymph, it is necessary to assume a difference in chemical composition between the two. The differences assumed are such as to give the greatest surface tension—about 60 dynes per cm. The composition of the two solutions cannot be varied sufficiently to give a surface tension anywhere near 6000 dynes per cm., which is the surface tension between certain forms of living matter and water, according to Jensen and Macallum.

The conditions in a working striated muscle, as just described, can be theoretically pictured as follows: Immediately before the contraction phase begins the lateral surfaces of the contractil units or muscle rods are covered with saturated sodium chlorid solution. Immediately in contact with this is the adjacent lymph consisting of a concentrated solution of butyric acid. Under these conditions the contraction begins with a surface tension of 60 dynes per cm., provided, as already pointed out, these maximum and minimum values occur simultaneously and at the beginning of the contraction phase.

If the contraction began under the driving force of 85 dynes per

cm., and if this were maintained thruout the entire contraction phase, and if striated muscle were a mechanism having an efficiency of 100 per cent., then the surface energy in 1 cc. of muscle would enable it to lift a little over 1000 grams<sup>23</sup> and surface energy might be regarded as the cause of muscle contraction.

The efficiency of the muscles of the human body as a machine is very close to 21 per cent.,<sup>24</sup> and it is almost certain that if any of the driving force in striated muscle is due to surface tension at all, the tension is but a small fraction of 85 dynes. The above figures should be interpreted accordingly.

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<sup>23</sup> Berg: BIOCHEMICAL BULLETIN, 1912, ii, p. 109. The value, 361 grams, is to be multiplied by 3.1416, the value of  $\pi$  having been accidentally omitted. The correct figure is, therefore, 1134 grams.

<sup>24</sup> Benedict and Carpenter: *Bulletin* 208, *Office of Experiment Stations, U. S. Dept. of Agric.*, 1909, pp. 1-44. Hill: *Jour. of Physiol.*, 1913, xlv, pp. 435-469.

## THE PHYSICO-CHEMICAL BASIS OF STRIATED-MUSCLE CONTRACTION

### 4. Sources of surface tension in striated muscle

WILLIAM N. BERG

Thruout the works of Bernstein, Jensen and Macallum on muscle contraction, the assumption is made (or implied) that the chemical changes taking place in an active muscle are such as to give rise to a surface tension between the contractil unit and the adjacent lymph, as if a difference in chemical composition or in concentration between two adjacent regions necessarily causes surface tension. Which chemical reactions in muscle can cause surface tension between contractil unit and adjacent lymph? That there are very few such reactions will, perhaps, be apparent from the following data on the surface tensions of aqueous solutions of biological substances.

Suppose two adjacent regions in a living cell to differ in their chemical composition. Will there be an osmotic difference between the two? The answer is that this will depend upon the nature of the difference in composition. If the two regions differ only in the fact that there is more protein present in one than in the other, there will be no osmotic difference, or the difference will be a negligible one. But if the regions differ in their concentrations of electrolytes, or of organic substances of relatively low molecular weight, there will be an osmotic difference which may be very great. That is to say, some solutes exert osmotic pressure, others do not. The same is true of solutes with regard to surface tension. *Whether a difference in chemical composition or concentration between two adjacent regions necessarily involves surface tension depends upon the nature of the solute.*

For the present purpose, most solutions of biological substances may be considered as falling into one of the following three classes. (Certain data on the surface tension of these types of solutions will

be considered with reference to their bearing on the problem of the sources of surface tension in living matter in general and in striated muscle in particular.) The first class of solutions to be considered are those which are obtained when two partly miscible liquids, such as ether and water, for example, are thoroly shaken, and then allowed to separate into two layers, forming in this case, a solution of water in ether and a solution of ether in water. The surface tension between two such layers is of interest for several reasons, principally because such binary mixtures probably exist in living tissue, which is supposed to consist of a comparatively dilute aqueous solution or suspension of the biological constituents that bathes the more viscous protoplasmic structures. These structures, whatever their shape and size may be, are commonly regarded as solutions of water in the biological constituents.

The surface tension between two liquids was studied by Quincke in 1870.<sup>1</sup> He found that the surface tension between two liquids, immediately after they have come in contact, is very nearly equal to the difference between their surface tensions when measured separately against air. For example, the surface tension of chloroform against air is 30.6 dynes per cm., that of water against air is 80.9; the surface tension between chloroform and water is approximately the difference between these two figures, or 29.5 dynes per cm. If the two liquids were mutually soluble, the surface tension between the two decreast to an extent which depended upon their mutual solubility and other factors. The following typical data, from Quincke's paper, are of interest because the general principle deduced from them by Quincke is directly applicable to the conditions existing in a working muscle (on the assumption that the chemical and physical changes underlying muscle contraction take place between solutions or other liquids and not between solutions and gases).

Quincke, loc. cit., p. 27. Table X. Results at 20° C. in dynes per cm. In the first column of figures is given the surface tension of the first liquid against air; in the second column, the surface tension of the

<sup>1</sup> Quincke: *Annalen der Physik und Chemie*, 1870, cxxxix, pp. 1-89. (*Pogendorff's Annalen*.)



second liquid against air; in the third column, the surface tension between the two liquids as actually determined.<sup>2</sup>

Carbon disulfid-water . . . . .	32.0	80.9	41.7
Petroleum-water . . . . .	31.7	80.9	37.6
Chloroform-water . . . . .	30.6	80.9	29.5
Olive oil-water . . . . .	36.8	80.9	20.5
Turpentine-water . . . . .	29.7	80.9	11.5
Olive oil-alcohol . . . . .	36.8	25.5	2.2

Quincke concluded that the surface tension between two liquids that do not react chemically, of course, is not quite equal to the difference between their surface tensions when measured separately against air, and that it varies between this difference and zero, according to the mutual solubility, etc., of the two liquids (p. 18). This principle is important, because the surface tensions between solutions probably existing in muscle can be easily calculated, if the surface tensions of these solutions have been measured against air. A direct measurement of the surface tension between contractile unit and adjacent lymph is, therefore, not absolutely necessary.

Antonow<sup>3</sup> measured the surface tension between water and a second liquid, such as chloroform, ether, etc., practically repeating some of Quincke's work, with the same result, *i. e.*, the surface tension between two liquids is equal to the difference between their surface tensions when measured separately against air (p. 384).

In certain cases, studied by Whatmough<sup>4</sup> and by Antonow,<sup>5</sup> the mutual solubility of the two liquids may be great enough to bring the surface tension down to zero or very near to it, while the two liquids still differ greatly in their composition. Whatmough (p. 178) studied the surface tensions of several binary mixtures, such as phenol and water, isobutyric acid and water, etc. In his experiments, the two liquids were thoroly mixt, allowed to separate into layers, and then portions of the upper and of the lower layers were separately removed and their surface tensions against air deter-

<sup>2</sup> An extremely interesting and detailed summary of data on surface tensions of solutions, etc., was also given by Castell-Evans: *Physico-chemical Tables*, ii, pp. 708-801 (London, 1911).

<sup>3</sup> Antonow: *Journal de chimie physique*, 1907, v, pp. 362-385.

<sup>4</sup> Whatmough: *Ztschr. f. physikal. Chem.*, 1901, xxxix, pp. 129-193.

<sup>5</sup> Antonow: *Loc. cit.*

mined. The following results are typical of many others obtained by Whatmough (p. 181).<sup>6</sup>

*Phenol and Water*

25 ° C.	100 gm. water layer contain	8.5 gm. phenol	42.5 dynes/cm.
40 ° C.	100 gm. water layer contain	9.6 gm. phenol	41.1 dynes/cm.
20 ° C.	100 gm. phenol layer contain	72.1 gm. phenol	42.4 dynes/cm.
40 ° C.	100 gm. phenol layer contain	66.9 gm. phenol	40.6 dynes/cm.

*Anilin and Water*

35 ° C.	100 gm. water layer contain	3.4 gm. anilin	57.0 dynes/cm.
35 ° C.	100 gm. anilin layer contain	95.1 gm. anilin	51.6 dynes/cm.

*Isobutyric Acid and Water*

6.5° C.	100 gm. water layer contain	16.4 gm. isobutyric acid	29.9 dynes/cm.
25.2° C.	100 gm. water layer contain	36.3 gm. isobutyric acid	28.4 dynes/cm.
6.0° C.	100 gm. acid layer contain	73.4 gm. isobutyric acid	29.6 dynes/cm.
25.2° C.	100 gm. acid layer contain	36.3 gm. isobutyric acid	28.4 dynes/cm.

From the above data it is evident that two aqueous solutions in contact with one another may differ greatly in their concentration of a common solute, with a very small surface tension between them. In the above cases, the surface tension between the phenol and water solutions is practically zero and the same is true of the isobutyric acid solutions. Between the water solution of anilin and the anilin solution of water there is a surface tension of but 5.4 dynes per cm., altho the two layers differ in the fact that one contains 3.4 per cent. of anilin; the other, 95 per cent. In all of the above cases the layers are in equilibrium insofar as the layers can remain in contact indefinitely, without changing their concentrations, so long as the temperature and other conditions remain constant.

Whatmough did not measure the surface tension of one layer against the other; this was done by Antonow<sup>7</sup> shortly after. According to Antonow, the two layers obtained, for example, by thoroly mixing isobutyric acid and water, and then allowing the layers to separate, have exactly the same surface tension against air (p. 370). The surface tension between these layers would be zero. The slight differences between the surface tensions of the

<sup>6</sup> Data on solubilities taken from Seidell: *Solubilities of Inorganic and Organic Substances* (New York, 1911).

<sup>7</sup> Antonow: *Journal de chimie physique*, 1907, v, pp. 362-385.

two layers measured against air by Whatmough are due to experimental error, according to Antonow. His experimental results and conclusions are practically identical with those of Quincke and Whatmough already quoted.

For the present purpose these works of Quincke, Whatmough and Antonow may be summarized as follows: (1) The surface tension between two partly immiscible liquids is equal to the difference between their surface tensions against air.<sup>8</sup> (2) If the two liquids are mutually soluble tho not miscible in all proportions, the surface tension between the two layers is less than the above difference, and in some cases (water-phenol, water-isobutyric acid, methyl alcohol-carbon disulfid, etc.) it is zero. (3) Aqueous solutions of phenol, isobutyric acid and other substances, such as tartaric, citric and oxalic acids, to be considered later, may vary greatly in their concentration with very little variation in their surface tension.

The second class of solutions to be considered are the aqueous solutions of organic substances in general. Water has a higher surface tension than any organic liquid. The exceptional physical properties of water manifest themselves here, as in other branches of physics. The result is that, with the few exceptions to be noted presently, practically all solutions of organic substances have surface tensions lower than that of water.<sup>9</sup> The general relation between concentration of organic substance and surface tension is illustrated by the following curve for butyric acid and water. Butyric acid is taken as an example; a very large number of other organic substances depress the surface tension of water in a similar manner.

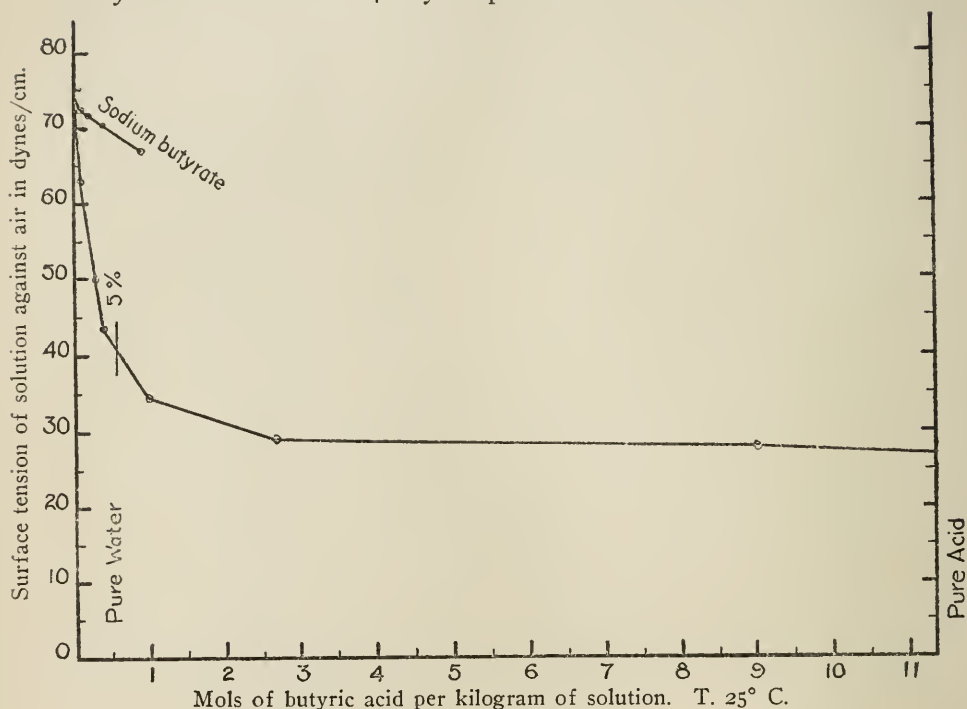
The following points about the nature of the curve are of interest: (1) A small amount of the organic substance lowers the surface tension of water a great deal.<sup>10</sup> (2) As the concentration of organic substance varies from approximately 20 to 100 per cent., the surface tension remains practically the same.

<sup>8</sup> Vernon (*Biochem. Ztschr.*, 1913, li, p. 1) quotes Maxwell to the effect that this is not true. But Maxwell's statement apparently was made before the work of Quincke was done.

<sup>9</sup> Freundlich: *Kapillarchemie*, p. 58 (Leipzig, 1909).

<sup>10</sup> On the other hand, no amount of any substance can raise the surface tension of water very much. Gibbs: *Thermodynamic Studies*, p. 321; cited from Freundlich, loc. cit., p. 57.

Suppose two adjacent regions, *A* and *B*, in a living muscle for example, to differ in the fact that *A* is pure water and *B* is a 5 per cent. solution of butyric acid in water. What is the surface tension between them? From the curve it is evident that the surface tension of pure water against air is 74 dynes per cm., that of a 5 per cent. butyric acid solution is 40 dynes per cm. The surface tension be-



The lower curve was obtained by plotting the figures of Drucker (*Ztschr. f. physikal. Chem.*, 1905, lii, p. 641) obtained from Freundlich (*Kapillarchemie*, p. 59; Leipzig, 1909).

The upper curve, for sodium butyrate, was obtained from Forch (*Annalen der Physik und Chemie*, 1899, lxxviii, p. 801).

tween *A* and *B* would, therefore, be the difference between the two, or 34 dynes per cm. But suppose that *A* and *B* differ in the fact that *A* contains 25 per cent. and *B* anywhere up to 100 per cent. of butyric acid. There would be practically no surface tension between the two, altho the difference in concentration is very great. For the present it is immaterial how the difference in concentration is brought about. The blood-lymph might bring equal amounts of

butyric acid or other organic substance to *A* and *B*. As a result of a continued tho unequal rate of combustion between *A* and *B*, the concentration of the metabolite might be continually different between the two regions and still cause no surface tension, unless, as a special case, that difference happens to be one between low concentrations. The point to be emphasized is that surface tension is caused by special and not by general differences in concentration of organic metabolites.

Of course, there are some organic substances that affect the surface tension of water very little, and consequently no surface tension changes would be brought about in those regions where they are being metabolized. As examples of such substances, tartaric, citric and oxalic acids may be mentioned. Aqueous solutions of these acids, even of high concentration, differ very little in their surface tension from that of pure water, as indicated by the following data from Linebarger.<sup>11</sup>

	Per cent of acid	Surface tension; dynes/cm., 15°C.
Water (pure) .....	0.00	71.27
Tartaric acid .....	18.18	71.44
Tartaric acid .....	53.32	73.86
Citric acid .....	6.12	69.35
Citric acid .....	5.08	65.19
Oxalic acid .....	1.53	70.65
Oxalic acid .....	9.13	69.85

Two adjacent regions would have practically no surface tension between them if one were water and the other an aqueous solution of tartaric acid of practically any concentration. The same is true for the other two acids.

By an accurate method, Morgan and Woodward<sup>12</sup> (p. 1256) found the surface tension of blood and blood serum to be 45.4 dynes per cm. at 37° C.; their value for water is 69.84. The figures are mentioned here for comparative purposes.

The third class of solutions to be considered are the aqueous solutions of the inorganic salts present in biological solutions. Can these be regarded as sources of surface energy? This is doubtful

<sup>11</sup> Linebarger: *Jour. Amer. Chem. Soc.*, 1898, xx, pp. 128-130. For data on the salts of these acids see Morgan and McKirahan: *Jour. Amer. Chem. Soc.*, 1913, xxxv, pp. 1759-1767.

<sup>12</sup> Morgan and Woodward: *Jour. Amer. Chem. Soc.*, 1913, xxxv, pp. 1249-1262.



because the inorganic salts enter the living system and leave it in practically the same condition—they do not undergo combustion or any other chemical change by which appreciable quantities of energy are derived from them.<sup>13</sup> For the present they might be regarded like the water and the lubricating oil in a steam engine—both oil and water are necessary, but neither are sources of energy. But the argument might be made that altho the inorganic salts are not sources of energy, they transform energy liberated in the metabolic processes into surface energy. For this reason the limiting values for aqueous solutions of inorganic salts are of interest. In general, the surface tension of inorganic-salt solutions is higher than that of water, but the difference is not great, even for concentrated solutions.<sup>14</sup> The inorganic salts raise the surface tension of water by an amount approximately proportional to their concentration. The upper limit for the surface tension of an aqueous salt solution is very near 85 dynes per cm.<sup>15</sup> Landolt-Börnstein<sup>16</sup> record some values higher than this for concentrated solutions of sodium hydroxid (99.7 dynes) and potassium carbonate (107 dynes). Since such solutions do not exist in living matter these values will be disregarded.

Therefore, if two adjacent regions in a living muscle differed in the fact that one was pure water and the other a saturated aqueous solution of sodium chlorid or of any other salt present in living tissue, the surface tension between them might be as high as 10 dynes per cm., which is the difference between the surface tension of water (75 dynes) and of saturated sodium chlorid solution (85 dynes), both measured separately against air at ordinary temperatures.

There are, of course, still other classes of solutions; but the three classes discusst are sufficient to definitely locate the upper and lower limits of the surface tension in striated muscle. Of course, the actual surface-tension changes are unknown at present.

<sup>13</sup> Sherman: *Chemistry of Food and Nutrition*, p. 260 (New York, 1911).

<sup>14</sup> Heydweiler: *Ann. d. Physik.*, 1910, xxxiii, p. 181. Lewis: *Ztschr. f. physikal. Chem.*, 1910, lxxiv, p. 619. Freundlich: *Kapillarchemie*, p. 62 (Leipzig, 1909). Morgan and Bole: *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 1750.

<sup>15</sup> Forch: *Annalen der Physik.*, 1905, xvii, p. 744-762.

<sup>16</sup> Landolt-Börnstein: *Physikalisch-chemische Tabellen*, 4te Aufl., pp. 128, 129 (Berlin, 1912). Castell-Evans: *Physico-chemical Tables*, ii, p. 768 (London, 1911).

To summarize: The conditions existing in a living muscle are not such as to give rise to any very great surface tension between two adjacent regions. A surface tension of about 62 dynes between contractil solution and adjacent lymph is obtained by assuming that at the beginning of the contraction phase, the contractil unit is bathed by a saturated aqueous solution of an inorganic salt, having a maximum surface tension of 85 dynes, and immediately in contact with this is the adjacent lymph, consisting of a dilute aqueous solution of an organic substance having a minimal surface tension of about 23 dynes/cm. But, as pointed out before, there is no particular reason for assuming that these values exist coincidentally, or that they exist at all in muscle. The maximum value at the beginning of the contraction is therefore, theoretically, not far from 62 dynes per cm. This may be entirely sufficient to account for the movement of salts, secretions, etc., but it is entirely insufficient to account for the lifting power of muscle, as indicated by our calculations already published<sup>17</sup> and recently corrected (see p. 179).

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<sup>17</sup> Berg: BIOCHEMICAL BULLETIN, 1912, ii, p. 109.

## RESEARCHES ON THE PHYSICO-CHEMICAL PROPERTIES OF VEGETABLE SAPS

### 2. Note on a comparison of the physico-chemical constants of the juice of apples and pears of varying size and fertility<sup>1</sup>

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(WITH PLATE 2)

**Introduction.** The problem of the relationship between pollination and the development of the ovary has been treated by various botanists, Ewart, Fitting, Müller-Thurgau, Moll, Solacolu, Treub, and by one of us.

That there is a distinct correlation between the number of seeds and the size of the fruit in which they are produced, and that this interdependence is independent of the correlation between the number of ovules formed and the size of the fruit, and that it is probably not due to both the ovules and the fruit having been exposed to like nutritional conditions was, we believe, first demonstrated by one of us.<sup>2</sup>

The nature of this relationship, which is probably a more or less direct causal one with fertility as the independent and size attained by the fruit as the dependent variable, is quite unknown. Naturally the suggestion arises that it is of the nature of a hormone. Certainly the most promising lines of research in the attempt to explain such correlations as those demonstrated between fertility (seed production) and the size of the fruit in *Cercis* and *Staphylea* would seem to lie in the direction of determining whether fruits which differ in fertility also differ in chemical composition. *A priori* it might seem possible that the mechanism by which variations in size

<sup>1</sup> For the first paper in this series see *Bull. Torrey Bot. Club*, 40, 27-34; 1913.

<sup>2</sup> Harris, J. Arthur: *Bot. Gaz.*, 50, 117-127; 1910. *Ibid.*, 53, 204-218, 396-414; 1912.

of fruit would follow upon variations in fertility would be osmotic in nature. For a final answer to these questions one should carry out series of determinations upon immature fruits with various numbers of seeds. This we have not as yet been able to do. In the meantime it may not be out of place to call attention briefly to certain negative results which we have obtained with practically ripe fruits of apple and pear.

These pomes are well adapted to such studies. An abundance of fruit can be obtained from a single tree, the seeds are not too many and are easily counted, the weight of the individual fruits is conveniently large, and their juice is easily expressed and analysed. Our materials were drawn from a single apple tree, apparently a seedling, and from a single pear tree producing medium sized fruits. Thus in so far as homogeneity can be assured by having all the fruits dealt with from the same individual tree, our materials are beyond criticism.

The samples were frozen before the sap was expressed.<sup>3</sup> The calculation of the constants of the juice was carried out according to the conventional formulae, correction being made for the undercooling in the case of the freezing point depression.

TABLE I

*Relationship between number of seeds and weight of fruit in pears*

Seeds per fruit	Lot 1		Lot 2		Combined series		
	<i>f</i>	Total weight in grams	<i>f</i>	Total weight in grams	<i>f</i>	Total weight in grams	Mean weight
1	3	204	4	250	7	454	64.86
2	7	408	17	1,172	24	1,580	65.83
3	13	776	11	911	24	1,687	70.29
4	10	661	16	1,325	26	1,986	76.38
5	17	1,161	17	1,351	34	2,512	73.88
6	16	1,042	25	2,036	41	3,078	75.07
7	20	1,428	19	1,703	39	3,131	80.28
8	40	3,052	23	2,094	63	5,146	81.68
9	17	1,355	29	2,572	46	3,927	85.36
10	18	1,392	12	1,168	30	2,560	85.33

**Statement of results.** The first question to be solved: Is there, in apples and in pears, a correlation between the number of

<sup>3</sup> Gortner and Harris: Notes on the Technique of the Determination of the Depression of the Freezing Point, *Plant World*, 17, 49-53; 1914.

TABLE 2

*Relationship between number of seeds and weight of fruit in apples*

Seeds per fruit	<i>f</i>	Total weight in grams	Mean weight
4	4	184	46.00
5	18	892	49.56
6	37	1,838	49.67
7	35	1,803	51.51
8	46	2,328	50.60
9	46	2,369	51.50
10	14	752	53.71
11	6	353	58.83
12	3	163	54.33
15	1	85	85.00

TABLE 3

*Weight in grams of apples (A) and pears (P<sub>1</sub>=Lot 1, P<sub>2</sub>=Lot 2)*

Weight	A	P <sub>1</sub>	P <sub>2</sub>	Weight	A	P <sub>1</sub>	P <sub>2</sub>	Weight	A	P <sub>1</sub>	P <sub>2</sub>
29	1	—	—	64	7	4	1	97	—	3	1
33	—	1	—	65	—	5	8	98	—	3	5
34	2	—	—	66	1	4	4	99	—	2	3
35	—	—	—	67	—	4	2	100	—	1	2
36	3	—	—	68	2	5	4	101	—	—	1
37	6	—	—	69	1	2	6	102	—	—	4
38	5	1	—	70	1	3	2	103	—	—	4
39	7	1	—	71	1	4	2	105	—	2	3
40	4	—	—	72	1	2	3	106	—	1	2
41	7	—	—	73	1	4	2	107	—	—	4
42	5	—	1	74	1	3	2	108	—	2	2
43	6	—	—	75	—	3	8	109	—	—	1
44	6	1	1	76	—	4	1	110	—	—	1
45	8	1	—	77	—	3	5	111	—	—	1
46	5	—	—	78	—	5	3	112	—	—	—
47	6	2	—	79	2	3	3	113	—	1	1
48	16	4	1	80	1	2	1	114	—	—	—
49	7	2	—	81	—	2	2	115	—	—	1
50	10	1	1	82	—	3	3	116	—	—	—
51	10	3	—	83	—	1	3	117	—	—	1
52	13	1	—	84	—	—	4	118	—	—	1
53	8	2	1	85	1	1	4	119	—	—	—
54	5	4	1	86	—	4	1	120	—	—	1
55	9	2	1	87	—	3	3	121	—	—	—
56	8	3	1	88	1	2	2	122	—	—	—
57	5	5	1	89	—	6	5	123	—	—	—
58	7	4	1	90	—	1	6	124	—	—	2
59	5	2	—	91	—	1	4	125	—	—	—
60	6	5	—	92	—	2	3	126	—	—	1
61	4	2	2	94	—	1	5	127	—	—	1
62	3	5	4	95	—	1	4	128	—	—	—
63	2	5	3	96	—	1	4	129	—	—	1

seeds produced and the size to which the fruit attains, such as has been demonstrated in *Cercis* and *Staphylea*? Ewart,<sup>4</sup> on the basis

<sup>4</sup> Ewart, R.: *Landwirtschaftl. Jahrb.*, 35; 1906.



of a small series of apples, affirms that there is. The condensed<sup>5</sup> correlation table (1) gives the relationship between the number of seeds per fruit and the weight in two collections of pears. Table 2 presents the data for apples. To complete the calculation of  $r$  from these tables the distributions of the weight of the fruits are necessary. The data are given in Table 3.

From these data we deduce for pears, Lot 1:

$$\begin{array}{ll} \bar{s} = 6.646, & \sigma_s = 2.384, \\ \bar{w} = 71.298, & \sigma_w = 16.204, \end{array}$$

whence

$$r_{sw} = +0.368$$

or, expressing in terms of linear regression of weight in grams on seed number according to the usual equation,

$$w = \left( \bar{w} - r \frac{\sigma_w}{\sigma_s} \bar{s} \right) + r \frac{\sigma_w}{\sigma_s} s,$$

$$w = 54.684 + 2.500 s.$$

For pears, Lot 2:

$$\begin{array}{ll} \bar{s} = 6.173, & \sigma_s = 2.534, \\ \bar{w} = 84.289, & \sigma_w = 17.640, \\ r_{sw} = +0.398. \end{array}$$

For pears, both series:

$$\begin{array}{ll} \bar{s} = 6.401, & \sigma_s = 2.474, \\ \bar{w} = 78.027, & \sigma_w = 18.162, \\ r_{sw} = +0.323, & w = 62.829 + 2.374 s. \end{array}$$

For apples:

$$\begin{array}{ll} \bar{s} = 7.676, & \sigma_s = 1.746, \\ \bar{w} = 51.271, & \sigma_w = 9.754, \\ r_{sw} = +0.217, & w = 41.982 + 1.210 s. \end{array}$$

Thus there is in all these cases a material correlation between the number of seeds matured and the weight attained by the fruit. These results confirm the conclusions of Ewart for apples and of Harris for *Cercis* and *Staphylea*.

<sup>5</sup> Harris, J. Arthur: *Amer. Nat.*, 43, 693-699; 1910.

The physico-chemical constants determined for these series appear in Table 4-5. For the fertility series they are compared with the slope of the regression line calculated by the above equation for

TABLE 4

*A. Constants for juice of pears producing various numbers of seeds*

No. of seeds	Specific gravity $d_{20}^{20}$	Concentration solids solute	Corrected depression of freezing point $\Delta$	Mean molecular weight $M$	Osmotic pressure $P$	Specific conductivity $\kappa$
2	1.0476	0.1315	1.325	187.6	15.94	0.00318
3	1.0483	.1328	1.352	185.5	16.26	.00343
4	1.0474	.1290	1.321	184.5	15.89	.00370
5	1.0478	.1328	1.318	190.4	15.85	.00344
6	1.0473	.1294	1.301	188.0	15.65	.00352
7	1.0475	.1288	1.311	185.7	15.77	.00347
8	1.0468	.1282	1.291	187.7	15.53	.00354
9	1.0466	.1280	1.299	186.2	15.63	.00367
10	1.0466	.1262	1.289	185.0	15.51	.00357

*B. Constants for juice of apples producing various numbers of seeds*

4	1.0402	0.1136	1.166	185.1	14.93	0.00163
5	1.0396	.1058	1.083	184.6	13.03	.00278
6	1.0397	.1068	0.880 <sup>6</sup>	229.4	10.59	.00267
7	1.0403	.1091	1.088	188.5	13.09	.00266
8	1.0400	.1074	1.098	184.9	13.21	.00266
9	1.0390	.1045	1.059	186.5	12.74	.00272
10	1.0403	.1090	1.098	187.7	13.21	.00264
11	1.0393	.1038	1.085	180.7	13.06	.00273
12	1.0401	.1069	1.093	184.7	13.15	.00259

TABLE 5

*Constants for juice of pears of various weights in classes of 10-gram range*

Weight of fruit	Specific gravity $d_{20}^{20}$	Concentration solids solute	Corrected depression of freezing point $\Delta$	Mean molecular weight $M$	Osmotic pressure $P$	Specific conductivity $\kappa$
40-49	1.0479	0.1302	1.390	177.0	16.72	0.00303
50-59	1.0496	.1380	1.427	182.8	17.16	.00292
60-69	1.0521	.1388	1.470	178.5	17.68	.00312
70-79	1.0497	.1361	1.403	183.4	16.87	.00296
80-89	1.0500	.1370	1.412	183.3	16.98	.00298
90-99	1.0505	.1361	1.399	184.0	16.83	.00297
100-109	1.0501	.1356	1.392	184.1	16.74	.00284
110-119	1.0521	.1415	1.425	187.7	17.14	.00309
120-129	1.0505	.1388	1.444	181.7	17.37	.00295

<sup>6</sup> This value of  $\Delta$  is obviously erroneous, but the slip was not observed until it was too late to make another determination. It affects the mean molecular weight and the osmotic pressure.



DIAGRAM 1

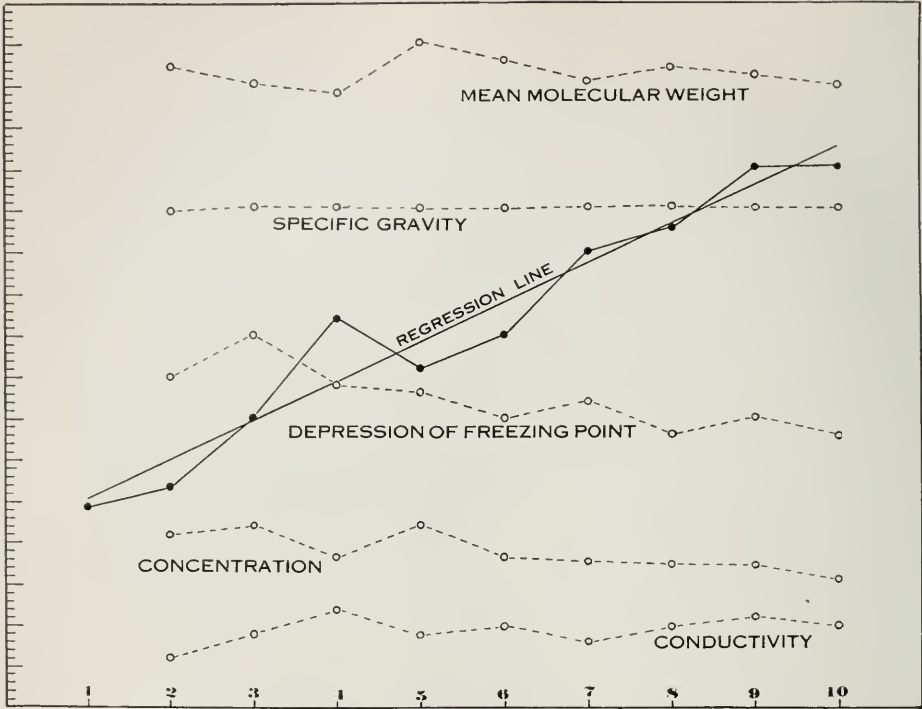
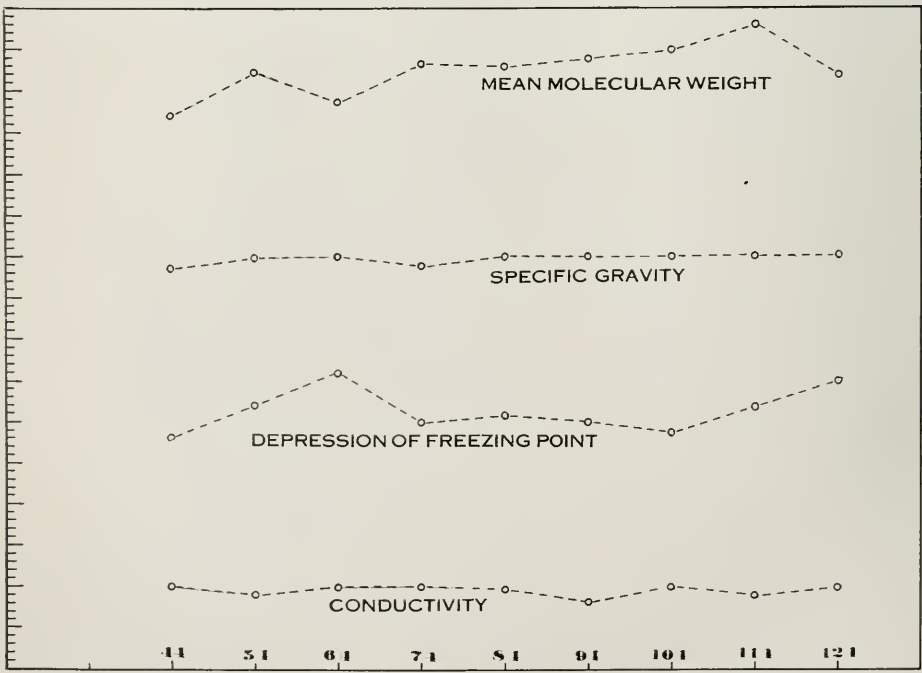


DIAGRAM 2



HARRIS AND GORTNER: COMPARISON OF PHYSICO-CHEMICAL  
CONSTANTS OF THE JUICES OF APPLES AND PEARS OF  
VARYING SIZE AND FERTILITY

the combined series in Diagram 1 (Plate 2). A comparison of these constants, both in the tables and in the graphs will, we believe, convince the reader that there is no close interdependence between either the weight (see Diagram 2) or the number of seeds (Diagram 1) of a pome and the physico-chemical properties of the expressed juices of practically matured fruit.

**Summary.** In apples and pears, as in *Cercis* and *Staphylea*, there is a material correlation between the size of the fruit and the number of seeds which it produces. Various considerations render it probable that the relationship is a direct causal one and that the size of the fruit is influenced by the number of seeds, rather than conversely.

The first suggestion concerning the mechanism of this relationship would seem to be that the development of the seeds influences in some way the physico-chemical properties of the sap in the developing fruit. We have, however, been unable to demonstrate any sensible differences in the osmotic pressure, mean molecular weight, or electric conductance of the saps of nearly ripe fruits of different sizes or producing different numbers of seeds. These findings do not preclude the possibility that in the earlier developmental stages of the fruit such differences may exist.

#### EXPLANATION OF DIAGRAMS, PLATE 2

*Diagram 1:* Comparison of physico-chemical constants of the sap of pears producing various numbers of seeds with the slope of the straight line (with empirical means) showing increase in weight of the fruit with increase in number of seeds per fruit.

*Diagram 2:* Physico-chemical constants of pears of various weights.

In neither case is there in the trend of the values any clear indication of relationship between the size of the fruit or the number of seeds which it produces and the constants determined. In both diagrams the significance of the scale to the left differs from constant to constant. The complete data are given in the tables.



# STUDIES OF PLANT GROWTH IN HEATED SOIL

GUY WEST WILSON

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(WITH PLATES 3-5)

**Introduction.** The problem of the effect of heat on soils is one of interest alike to the chemist and the botanist. The effect of heat on the soil elements themselves forms a prolific field for investigation, while the resultant changes in the growth of plants present a no less interesting series of problems. In a recent paper Seaver and Clark<sup>1</sup> have discussed some of the problems in each of these fields and presented a review of the literature of the subject to date. As the present paper represents work done in the same laboratory on the same line of problems, and following the same general methods of these workers, no further discussion of the previous work on the subject appears to be necessary, except in connection with the analysis of the results of the experiments detailed here.

**Experimental.** **GENERAL PLAN.** In all of the experiments described below the soil was the ordinary unfertilized soil of Bronx Park. While this is not rich in plant food and, from many standpoints, is not so satisfactory for such work as a richer agricultural soil, the results obtained from percolation experiments corresponded with those described by Seaver and Clark, except that the lighter color of the percolates indicated a lower percentage of soluble matter. For each experiment twelve four-inch pots were filled with sifted soil and divided into groups of three each. One group was used as the check and the others heated in a dry oven for two hours at temperatures of 95°, 135°, and 175° C., respectively. From each of these groups one pot was used for percolation and the others planted with the various crops to be grown, ten seeds being sown in

<sup>1</sup> Seaver, Fred J., and Clark, E. D.: Biochemical studies on soils subjected to dry heat, *BIOCHEM. BULL.*, 1: 413-427 (pl. 7); 1912.

each pot. After germination these were divided to form two complete series upon which observations were made. Photographs were made as developments suggested (Plates 3-5).

EXPERIMENT I. *Buckwheat*. The first culture was photographed when the seedlings were about four days old, again after the lapse of a week, and lastly at flowering time. A comparison of the photographs shows in the early part of the period of growth (Fig. 1) a slight acceleration in the pots heated to  $95^{\circ}$ , in the one heated to  $135^{\circ}$  it was somewhat retarded, and in the one heated to  $175^{\circ}$  there was marked retardation in germination and stunting in growth. The plants on the soil heated to the higher temperatures were increasingly more unhealthy in color and decreased in vigor. After the lapse of a week the same relative conditions were still apparent (Fig. 2). At flowering time the results were quite marked (Fig. 3). The plants in the pot heated to  $95^{\circ}$  came into bloom about five days earlier than did the check, and bloomed more profusely. The photograph was taken about a week after the first flowers appeared. At this time the check was second in vigor to the growth in the pot which had been subjected to a heat of  $95^{\circ}$ , while the plants on the soil heated to  $135^{\circ}$  lacked vigor and only one plant produced flowers, and that sparingly. The plants on the soil which had been heated to  $175^{\circ}$  produced no flowers, were of low vitality, and much stunted in growth. The following table shows in detail the results of this set of cultures.

Temperature of soil	Seeds germinated in 4 days	Seeds germinated in 11 days	Plants living at flowering time	Plants that flowered	Number of flowers produced
Check	8	8	8	4	11
$95^{\circ}$	8	8	8	6	12
$135^{\circ}$	5	7	6	1	4
$175^{\circ}$	3	6	3	0	0

From this it appears that, so far as buckwheat is concerned, slight heating of the soil is beneficial, while high heat retards growth very seriously, and produces weakened plants.

Checks were run on this experiment and the results agreed with those given above, except that none of the earlier cultures were kept until flowering time. No fungous disease appeared on the plants, although various fungi developed on the soil. While no especial

attention was given to these, it may be mentioned in this connection that the most abundant were *Pyronema* and a species of *Monilia*. A racemose species of *Mucor* appeared in one pot. These fungi did not appear to interfere with the germination of the buckwheat or of the small grains used in the other experiments of this series. The fungi were always more abundant on the soil which had been heated to the higher temperatures, while none appeared on the check pots.

EXPERIMENT II. *Wheat*. The first planting of wheat was allowed to grow about twelve days before being photographed (Fig. 5). The plants in all the pots showed good growth, there being a slight advantage with the check in vigor and color, while that in the soil which had been heated to the lowest temperature ( $95^{\circ}$ ) was almost as healthy and vigorous. In the two high temperature pots the growth was very rank and weak. Although not quite so tall, the plants in these two pots fell down or "lodged" considerably in the  $135^{\circ}$  pot, and very noticeably so in the  $175^{\circ}$  pot. The plants in these two pots behaved much as does grain grown on a soil too rich in humus. The later growth of this series, while not photographed, was quite interesting. The two low-temperature pots (check and  $95^{\circ}$ ) were almost equal in growth and vigor, the  $95^{\circ}$  one having a slight advantage in vigor and color, but not outgrowing the check in height. The other two pots remained stunted and, after the lapse of a month, showed appreciable inhibition as compared to the others. Indeed, the one which had been subjected to the highest temperature grew but little in height after the second week. This work was twice repeated with results similar to those just described.

One of these series was photographed at about five days after germination (Fig. 4). The plants on soil which had been heated to  $95^{\circ}$  showed a very slight advance over the check in color, but not quite such a good growth. The pot which had been subjected to a heat of  $135^{\circ}$  showed some retarded germination, giving a very uneven growth, while that subjected to a temperature of  $175^{\circ}$  was markedly retarded, showing only a slight growth as compared with the others. The work on wheat was seriously interfered with by rust (*Puccinia graminis*) and mildew (*Erysiphe graminis*), both of which attacked the weakened plants on the soils which had been heated to the higher temperatures in preference to the more vigor-

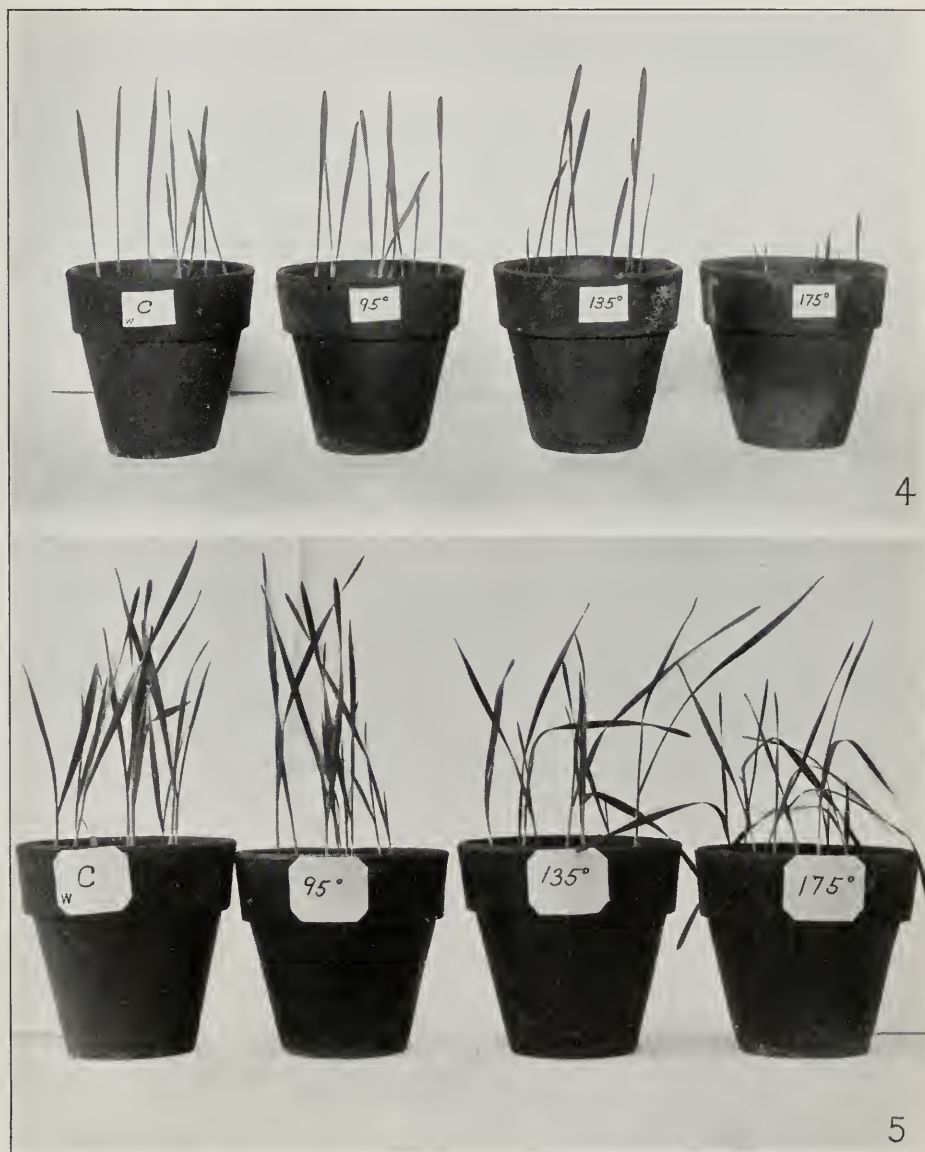


## WILSON: STUDIES OF PLANT GROWTH IN HEATED SOIL

*Fig. 1:* Buckwheat seedlings four days after germination; *Fig. 2:* Buckwheat seedlings one week older than those in *Fig. 1*; *Fig. 3:* Buckwheat at flowering time.



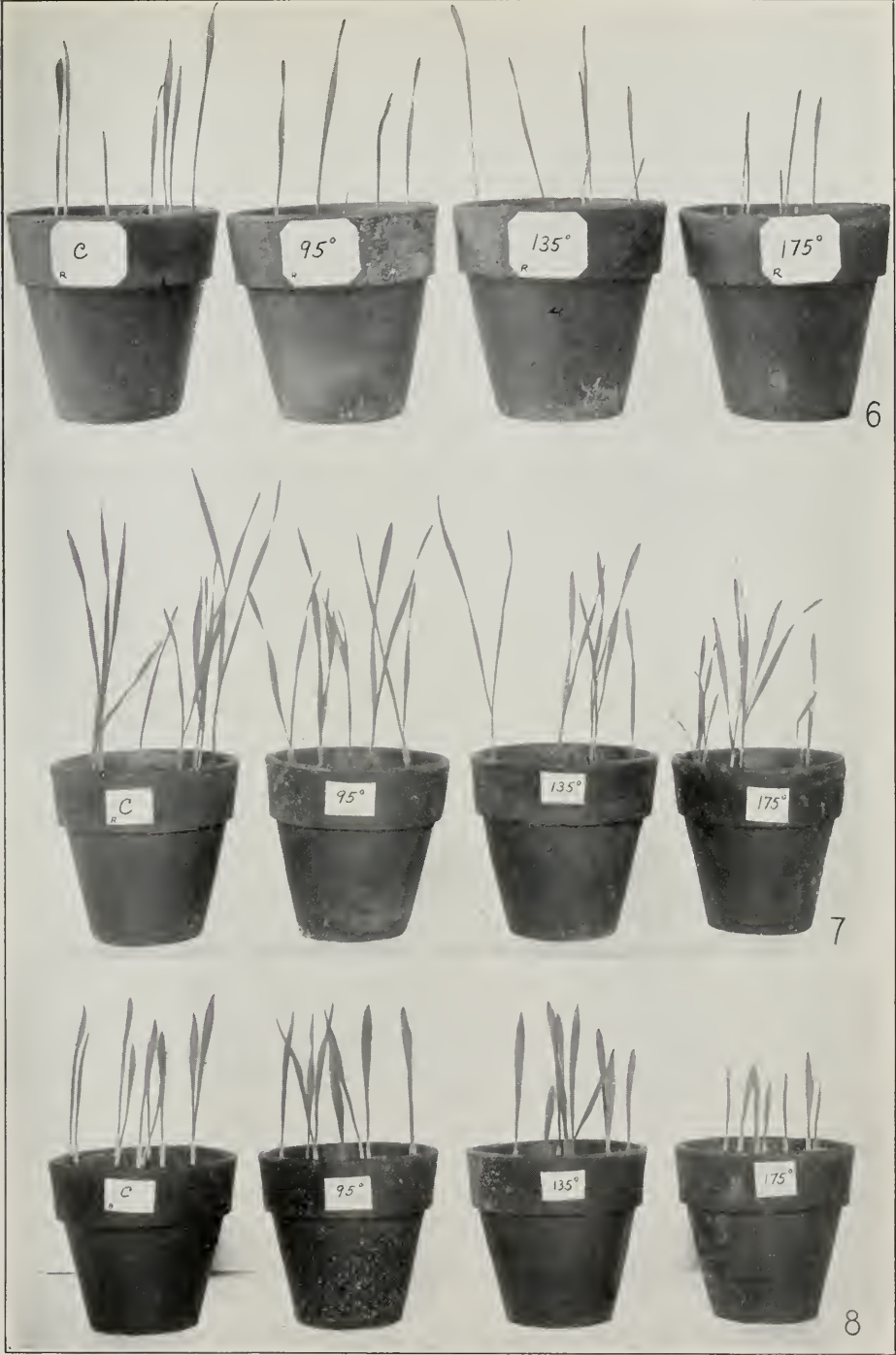




## WILSON: STUDIES OF PLANT GROWTH IN HEATED SOIL

*Fig. 4:* Wheat seedlings five days after germination; *Fig. 5:* Wheat seedlings from another culture two weeks old.





WILSON: STUDIES OF PLANT GROWTH IN HEATED SOIL

*Fig. 6:* Rye seedlings one week after germination; *Fig. 7:* Rye seedlings—the same culture after the lapse of one week; *Fig. 8:* Barley seedlings at the end of the first week.



ous plants on the lower heated soils. For this reason it was impracticable to keep the pots under observation until flowering time.

EXPERIMENT III. *Rye*. The plants in this experiment were first photographed at the end of a week (Fig. 6) and again at the end of the second week (Fig. 7). The plants were all very healthy, highly colored and sturdy. In the low-temperature pot ( $95^{\circ}$ ) the plants were slightly more colored than those of the check, and showed a better and more even growth. In the two higher-temperature pots the growth was retarded and the plants were weaker, but their heightened color showed the effect of the higher percentage of soluble matter in the soil on which they were grown. Germination was seriously retarded by heating to  $175^{\circ}$ . From the various cultures made of rye it would appear that there was a slight acceleration of growth on the soil subjected to a temperature of  $95^{\circ}$ , while the higher temperatures showed a proportionate retardation. These plants were severely attacked by mildew, those on the soils which had been heated to the higher temperatures suffering most seriously.

EXPERIMENT IV. *Barley*. At the end of the first week, when the barley plants were photographed (Fig. 8), germination was about equal in all the pots. The rate of growth varied considerably. The plants on the soil that had been heated to  $95^{\circ}$  were slightly taller than the check, those on the soil of the next member of the series ( $135^{\circ}$ ) were slightly retarded in growth, and those on the last one ( $175^{\circ}$ ) were markedly retarded in growth. While no repetition of this experiment was attempted, the results indicated that the growth of barley was affected less than that of any of the small grains grown in these soils, yet the highest temperature caused a serious retardation. It is probable that the optimum for barley is slightly higher than for the other plants which were used in this series of experiments.

**General discussion.** While the soil used in these experiments was, from the agricultural standpoint, a very poor loam, all the crops grown were those which might be considered best adapted to the type of soil used. Barley, alone of the series, is usually regarded as demanding a soil which might be termed rich, while buckwheat and rye are noted for their ability to grow on soils low in plant food. Wheat, however, demands a richer soil than the last named crops.



From the work of Seaver and Clark it appears that the materials rendered soluble by subjecting soil to dry heat show properties of sugars and organic acids; others have obtained results suggestive of soils composed almost entirely of humus, the acid nature of which is well known. It is possible that the preference of certain plants for peaty soils or burned-over areas may be due to the acidity of these soil types. Certain facts observed by the present writer in the course of the experiments described above, as well as field observations on the same crops in swamp soils which were very rich in humus, appear to bear out this theory. Buckwheat is usually grown on poor soil, where it thrives. The writer has seen a number of attempts to grow it on swamp land with uniformly unsatisfactory results. Comparable to this is the effect of subjecting the soil to a very high temperature. Wheat is also usually grown on a loamy soil of a rather low humus content as compared with swamp lands. When grown on the latter it has a tendency to produce weak stems with a consequent "lodging" of the grain. This is at least true in regard to certain varieties. The behavior of the plants on the soils which had been subjected to the higher temperatures suggests analogous results, as the leaves were flaccid and lacking in normal rigidity.

Throughout the entire series of experiments delayed germination and retarded growth characterized all the crops grown on soil subjected to a temperature of  $175^{\circ}$ . These results were quite marked. Similar results, but in a less pronounced degree, were noted in cultures on soil heated to  $135^{\circ}$ . Not only was the growth of these plants retarded, but their susceptibility to disease was increased.

The writer's experiments agree with those of Seaver and Clark in indicating that soils subjected to a low degree of heat ( $120^{\circ}$  C., or less) show an accelerated growth of green plants and a retardation of fungous growth, while soils heated to a higher temperature give results which are the reverse, *i. e.*, retarded growth of green plants and accelerated growth of fungi. These results also accord in the main with more recently published results obtained by other workers, although on the surface some of these may appear to differ.

Schreiner and Lathrop<sup>2</sup> have conducted extensive studies on the chemistry of steam-heated soils and their relation to plant growth. They autoclaved the soil samples at a temperature of 135° C., and under a pressure of 30 pounds, for a period of three hours. As a result of this treatment they note increased amount of soluble matter in the soil extract and retarded plant growth, both of which are to be expected under the circumstances. All the materials found in unheated soils were present in the heated samples except nucleic acid which was broken down and united with some of the protein substances to form new compounds. The effect on plant growth is explained by the fact that while beneficial elements are present they are overbalanced by harmful compounds. Upon the balance of these elements, then, depends the results upon plant growth. "This balance is influenced by cultural treatment, fertilizers, liming, crop growth, or crop rotation, etc., as well as by steaming."

Articles have also appeared, from time to time, upon the effect of soil sterilization as practiced commercially. This is accomplished by forcing steam into the soil *in situ*. While the nominal temperature to which the soil is subjected by this treatment is quite high, there are great difficulties in the way of securing an even distribution of the steam in the soil-mass. The results are a very uneven sterilization, the after effects of which are quite different from those obtained by other methods where the penetration is subject to less fluctuation. In this type of sterilization the prime object is to rid the soil of the nematodes, insect pests, injurious fungi and bacteria which may have accumulated in it. From this standpoint the method of soil treatment is satisfactory in so far as it reduces the ravages of these pests on the subsequent crop.

A summary of our knowledge along these lines has recently been published by Stone,<sup>3</sup> who noted acceleration in the growth of lettuce and cantaloupes on steam-heated soil, when it was rich in organic matter, while the results were bad on poor soil. The gross effect of such treatment on plant growth is apparently analogous to that following subjection of the soil content of the plot to a more *evenly*

<sup>2</sup> Schreiner, O. S., and Lathrop, E. C.: The chemistry of steam-heated soils, *U. S. Dept. Agric., Soils Bull.*, 89: 1-37; 1912.

<sup>3</sup> Stone, G. E.: The present status of soil sterilization, *Ann. Rep., Mass. Agr. Expt. Sta.*, 24: 121-125 (pl. 1, 2); 1912.

*distributed* heat at a lower temperature. The effects of tillage are also to be taken into account as possibly causing a more equal distribution of the elements after steam sterilization. Stone expresses the opinion that the acceleration which he and others have noticed in the case of steam-sterilized soils in market gardening districts is due rather to the chemical changes within the soil than to any modification of its flora or fauna.

Lodge and Smith<sup>4</sup> have studied the effects of steam heat on soils in relation to the growth of bacteria as well as green plants. They used soil sterilized for 45 minutes under a pressure of 15 pounds of steam at a temperature of 125° C. Percolates of these soils were sown with *Bacillus subtilis*. Their experiments showed that where the soils were rich in organic matter steam heat increased subsequent bacterial growth, while in soils deficient in organic matter such growth was retarded. They report similar results with green plants, and emphasize the fact that in the soil used protozoans were not present to an appreciable extent.

Various attempts have been made to explain the observed effects of soil-heating upon subsequent plant growth. Russel and Hutchinson<sup>5</sup> attribute the changes observed by them to the destruction of the soil-inhabiting protozoa and the consequent greater activity of the soil bacteria. Lyon and Bizzell<sup>6</sup> hold, on the other hand, that the results are due entirely to the chemical changes in the soil itself. Bolley<sup>7</sup> concludes that the most important factor is the destruction of the fungi and bacteria which are present in the soil and which might produce disease in the crops grown. Seaver and Clark consider "that the whole question of the effects of heating soils is a very complex one and one in which the experimenter's interpretation of results depends upon his training and point of view; whether it be bacteriological, chemical or phytopathological. It is very

<sup>4</sup> Lodge, C. A., and Smith, R. G.: Influence of soil decoctions from sterilized soils upon bacterial growth, *Ann. Rep., Mass. Agr. Expt. Sta.*, 24: 126-134; 1912.

<sup>5</sup> Russel and Hutchinson: The effect of partial sterilization of soils on the production of plant food, *Jour. Agr. Sci.*, 3: 111-114; 1909.

<sup>6</sup> Lyon, T. L., and Bizzell, J. A.: Effect of steam sterilization on the water-soluble matter in soils, *Bull. Cornell Agr. Expt. Sta.*, 275; 1910.

<sup>7</sup> Bolley, H. L.: Interpretation of results in experimentation on cereal cropping methods after soil sterilization, *Science*, 33: 229-234; 1912.

likely that the truth of the matter lies somewhere on the borderlines of the three sciences indicated." Beyond this we are not at present prepared to go, save to remark that the widely divergent soils studied severally by these observers probably contained substances which justify the conclusions of each. If each of these investigators had studied all the soils referred to in these papers, the interpretation of the results obtained might have been more harmonious.

**Summary of general conclusions.** All the plants used in this work showed a slight acceleration of growth and vigor on soil which had been heated to a temperature of  $95^{\circ}$  C. In the case of buckwheat, acceleration was quite marked.

All the plants used in these experiments showed a retardation of growth on soils subjected to a heat of  $135^{\circ}$  or  $175^{\circ}$  C., the retardation being especially marked for plants grown on soil heated to the higher temperature.

Plants grown on heated soil were more susceptible to attack by parasitic fungi than those grown on unheated soil, although the susceptibility to such attacks did not increase proportionately as the growth of the host decreased.

Soil fungi grew more abundantly on the soils which had been subjected to high temperatures, in one instance seriously interfering with the experiment.

The effect of heating soils upon the crop grown varies with the temperature to which the soil is subjected, the kind of soil used, and the nature of the crop grown upon it.

In conclusion most hearty thanks are due to Professor William J. Gies, to Dr. Fred J. Seaver and to Dr. Ernest D. Clark for their suggestions and advice during the progress of the work.

## A REVIEW OF METHODS FOR THE ISOLATION AND IDENTIFICATION OF THE ORGANIC CONSTITUENTS OF SOILS

A. W. THOMAS

Various studies of growth in heated soils, conducted under Dr. Gies' guidance in this laboratory and at the N. Y. Botanical Garden, have indicated that soils subjected to high temperatures gain or lose in their capacity to sustain the growth of various plants and fungi (see the preceding paper).<sup>1</sup> Does high temperature increase, in soils, the proportion and availability of nutrients or does it merely decrease the toxic power of, or remove, contained deleterious agents? If nutrients are increased, in soils, by the application of high temperatures, are the nutrients organic substances or inorganic products?

With a view of ascertaining whether the proportions of some of the leading organic substances may be increased, in a soil, under such conditions, and whether organic substances are produced *de novo* or wholly removed, I have applied to a soil, at Dr. Gies' suggestion, the methods of Schreiner for the isolation and detection of organic constituents (see page 313 of this issue).<sup>2</sup> For the benefit of readers of the BIOCHEMICAL BULLETIN who may desire a brief and easily accessible summary of these valuable methods, I have prepared the following review of them.<sup>3</sup>

Five kilos of soil, carefully sifted through a 2 millimeter sieve to remove stones, roots, insects, etc., are treated in a glass stoppered bottle with 15 liters of a 2 per cent sol. of sodium hydroxide for 48 hours with frequent shaking for the first 40 hours.

<sup>1</sup> Wilson: BIOCHEMICAL BULLETIN, 1914, iii, p. 202.

<sup>2</sup> Thomas: BIOCHEMICAL BULLETIN, 1914, iii, p. 313.

<sup>3</sup> Schreiner and Shorey: Chemical nature of soil organic matter, *Bull. No. 74, U. S. Dep't of Agric.*, 1910; Schreiner and Shorey: Examination of soils for organic constituents, especially di-hydroxy stearic acid, *Bull. No. 80, U. S. Dep't of Agric.*, 1911.



The supernatant alkaline extract is decanted and (2)<sup>4</sup> about *three-fourths* of this dark colored extract is acidulated with nitric acid, taking care to add not more than a slight excess of acid (see page 216). The nitric acid must be fresh and free from lower oxides of nitrogen. This acidification precipitates the "humic acids" in flakes that soon settle under a clear yellow sol.

(3) The precipitate is collected on a filter paper and washed until free from acid, and, while still moist, is extracted with boiling alcohol until a color is no longer imparted to the alcohol. The extracted precipitate of humus and silicic acid is now discarded and (4) the alcohol solution is evaporated, maintaining the original volume by additions of water. After the alcohol is completely removed, the aqueous sol. is filtered and the filtrate discarded.

The residue (5) insoluble in water, which may contain resin acids, resin esters, fatty glycerides, paraffinic acid, lignoceric acid,  $\alpha$ -mono-hydroxy stearic acid, hentriacontane, agosterol, phytosterol and other substances not yet identified, is dried, powdered, and extracted with petroleum ether until all soluble matter has been removed. The residue insoluble in petroleum ether contains the resin acids and resin esters.

(6) After evaporation of the petroleum ether, the residue is taken up in hot alcohol and the alcohol sol. allowed to cool; the portion insoluble in cold alcohol containing hentriacontane, agosterol, phytosterol,  $\alpha$ -mono-hydroxy stearic acid and lignoceric acid (7) is saponified with alcoholic potassium hydroxide sol., evaporated to dryness and extracted with petroleum ether, which takes up hentriacontane,<sup>5</sup> agosterol<sup>6</sup> and phytosterol.<sup>7</sup> The petroleum ether sol. is filtered and evaporated. The three above-mentioned substances in the residue may be separated and identified by virtue of the difference in their chemical and physical properties (9).

*Hentriacontane*:  $C_{31}H_{64}$ ; m.p., 68° C.; sp.g. at melting point,

<sup>4</sup> The numerals in parenthesis refer to the sections in the summary at page 218.

<sup>5</sup> Schreiner and Shorey: Paraffin hydrocarbons in soils, *Journ. Amer. Chem. Soc.*, 1911, xxxiii, p. 81.

<sup>6</sup> Schreiner and Shorey: The presence of a cholesterol substance in soils, *ibid.*, 1909, xxxi, p. 116.

<sup>7</sup> Schreiner and Shorey: Cholesterol bodies in soils, *Journ. Biol. Chem.*, 1911, ix, p. 9.

0.780; readily soluble in petroleum ether, ether; difficultly soluble in hot alcohol; almost insoluble in cold alcohol; unaffected by fuming nitric acid; does not absorb bromine.

*Agrosterol*:  $C_{26}H_{44}O$ ; m.p.,  $237^{\circ} C.$ ; member of the cholesterol family; soluble in ether, chloroform; readily soluble in hot alcohol; difficultly soluble in cold alcohol; almost insoluble in water; gives Liebermann's cholesterol reaction, but does not give the violet colored residue that cholesterol yields when evaporated with conc. hydrochloric acid and ferric chloride, nor the red cholesterol reaction with chloroform and sulfuric acid.

*Phytosterol*:  $C_{26}H_{44}O + H_2O$ ; m.p.,  $135^{\circ} C.$ ; gives the Liebermann reaction and also the cholesterol reaction with chloroform and sulfuric acid; soluble in ether, chloroform and in alcohol, hot and cold.

(10) The portion (7) insoluble in petroleum ether is taken up in water, acidified to liberate the fatty acids and shaken with ether. The ether extract may contain  $\alpha$ -mono-hydroxy stearic acid and lignoceric acid.

*$\alpha$ -Mono-hydroxy stearic acid*:<sup>8</sup>  $C_{18}H_{36}O_3$ ; m.p.,  $84-85^{\circ} C.$ ; very soluble in petroleum ether, ether, hot alcohol; difficultly soluble in cold alcohol; insoluble in water; crystallizes in small irregular leaflets; by very slow cooling of the alcoholic solvent six sided plates may be obtained.

*Lignoceric acid*:<sup>8</sup>  $C_{24}H_{48}O_2$ ; m.p.,  $80-81^{\circ} C.$ ; soluble in petroleum ether, ether and hot alcohol; slightly soluble in cold alcohol; insoluble in water.

Both these acids dissolve in alkalis and may be reprecipitated by acidification of the aqueous solution.

(8) The cold alcoholic filtrate from (6) is precipitated with alcoholic lead acetate, filtered, and the precipitate (11), after being freed from lead salts by washing with alcohol, is suspended in alcohol and decomposed with hydrogen sulfide. The alcoholic sol., after being freed from hydrogen sulfide by boiling, contains *paraffinic acid*,<sup>9</sup> which may, upon slow evaporation of the solvent, be

<sup>8</sup> Schreiner and Shorey: Some acid constituents of soil humus, *Journ. Amer. Chem. Soc.*, 1910, xxxii, p. 1674.

<sup>9</sup> Pouchét: Action of nitric acid on paraffin, *Bull. Soc. Chim.*, 1875 (2), xxiii, p. 111.

crystallized in the form of waxy leaflets melting at 45–48° C. Its empirical formula is  $C_{24}H_{48}O_2$ .

(12) The filtrate from (8) is freed from lead salts by treatment with hydrogen sulfide and, on evaporation, *fatty glycerides* may be obtained.

(13) The original filtrate (2), is shaken out with ether and the ether sol. (14) evaporated in a beaker over about 75 c.c. of water. The water sol. may contain, besides di-hydroxy stearic acid, nitric acid and other compounds soluble in ether. The nitric acid is eliminated by repeated washing of the ether extract with water and subsequent evaporation of the ether, as before, over water. The water is boiled, conc. to a small volume and filtered while hot through a small wet paper, thus separating the di-hydroxy stearic acid<sup>10</sup> which is soluble in hot water from insoluble oily and resinous impurities. On cooling, and standing for several hours, the di-hydroxy stearic acid crystallizes out in star-like clusters of leaflets which can be identified with the microscope and from their melting point.

*Di-hydroxy stearic acid*:  $C_{18}H_{36}O_4$ ; m.p., 98–99° C.; very slightly soluble in cold water, quite soluble in hot water; very soluble in alcohol and ether; water sol. is acid to litmus and decomposes carbonates of barium and calcium; barium salt crystallizes in somewhat characteristic globular concretions of radiating structure; silver salt is amorphous and quite insoluble in water.

(15) The sol., after extraction with ether, is neutralized with sodium hydroxide and filtered. The precipitate which may be formed during the neutralization is saved for treatment under (25). The neutral filtrate is divided into three aliquot portions. One of them (16) is precipitated with lead acetate, which removes much coloring matter, and the precipitate is discarded. To the filtrate (17) ammonia is added until slightly alkaline, and the solution is filtered. The precipitate (18) is decomposed with hydrogen sulfide, filtered to remove lead sulfide, and the filtrate boiled down to a small volume. After cooling, three volumes of alcohol are added and the mixture is allowed to stand over night. If a gelatinous precipitate (19) be formed, it is filtered off, washed with alcohol, and tested for *pentosans*<sup>11</sup> by the following methods (A–C):

<sup>10</sup> Schreiner and Shorey: The isolation of di-hydroxy stearic acid from soils, *Journ. Amer. Chem. Soc.*, 1908, xxx, p. 1599.

<sup>11</sup> Shorey and Lathrop: Pentosans in soils, *ibid.*, 1910, xxxii, p. 1680.

A. A portion of the precipitate is boiled with a little conc. hydrochloric acid and a few crystals of orcin. If pentosans are present, a green color is produced. A drop of ferric chloride sol. assists in the development of the color. After a strong color has developed, amyl alcohol is added, which absorbs the color formed by the reaction of orcin and the pentosans.

B. Some of the precipitate is boiled for a minute with conc. hydrochloric acid and then a sol. of phloroglucin in hydrochloric acid sol. is added. If a red color is formed, changing to a violet red, which rapidly darkens due to a fine black precipitate, the presence of pentosans is indicated.

C. Xylan may be identified by treating with cadmium carbonate and bromine according to the method of Bertrand,<sup>12</sup> and obtaining the characteristic crystals of the double salt: cadmium xylonate and cadmium bromide.

(20) The alcoholic filtrate from (19) is taken up in a small volume of water, hydrochloric acid is added and the above tests applied for *pentose sugars*.

(21) A second portion of the neutral filtrate (15) is precipitated with silver nitrate and filtered. The precipitate (22) removes most of the color from the sol. It is washed to remove soluble silver salts, suspended in water and decomposed with hydrogen sulfide. The sol. is boiled to remove the excess of hydrogen sulfide, filtered and conc. If the filtrate is very dark, reprecipitation with silver nitrate will be necessary. After evaporation to a small volume, and subsequent standing, picoline carboxylic acid,<sup>13</sup> if present, will crystallize out.

*Picoline carboxylic acid*:  $C_7H_7NO_2$ ; slightly soluble in cold water, easily in hot water; slightly soluble in alcohol and almost insoluble in ether; crystallizes from water in oblique prisms with water of crystallization, which is lost at  $100^\circ C.$ ; from conc. sol., crystallizes in very thin superimposed plates, forming large scale-like masses and giving very brilliant color effects with polarized light; sublimes unchanged on heating in an open dish; does not melt in a capillary tube at  $300^\circ C.$ ; water sol. is acid to litmus;

<sup>12</sup> Bertrand: *Bull. Soc. Chim.*, 1891 (3), v, p. 556.

<sup>13</sup> Schreiner and Shorey: The isolation of picoline carboxylic acid from soils and its relation to soil fertility, *Journ. Amer. Chem. Soc.*, 1908, xxx, p. 1295.



when neutralized, does not give a precipitate with either barium chloride, calcium chloride, cadmium sulfate, or lead acetate; cupric acetate produces a bluish crystalline precipitate, insoluble in cold water; silver nitrate, a flocculent amorphous precipitate; by oxidation is converted into lutedinic acid, which melts at 239° C.

(23) To the filtrate from (21) dilute ammonium hydroxide sol. is added until precipitation ceases, care being taken not to add an excess. The sol. is filtered and the precipitate (24), after washing carefully with water, is suspended in water and decomposed with hydrogen sulfide, the sol. is boiled to remove the excess of hydrogen sulfide, filtered, concentrated and allowed to stand. Cytosine,<sup>14</sup> if present, will separate out in shining leaflets or scales.

*Cytosine*:  $C_4H_5N_3O + H_2O$ ; clear crystals, effloresce in the air, become opaque, do not melt at 300° C. but darken slightly; difficultly soluble in cold water, quite soluble in hot water; difficultly soluble in alcohol; insoluble in ether; water sol. is neutral, but compounds of definite crystalline appearance can be obtained with acids; sulfate crystallizes in needles, hydrochloride in prisms; forms a difficultly soluble picrate, crystallizing in needles; the chloroplatinate crystallizes in characteristic prisms; addition of potassium bismuth iodide to an acidified water sol., forms a red micro-crystalline precipitate.

(25) The neutralization precipitate from (15) is added to the third portion of the neutralized filtrate and made strongly alkaline with sodium hydroxide and filtered. To the boiling filtrate Fehling sol. is added, together with a little glucose. The sol., after the precipitation is complete, is filtered while hot and the filtrate discarded.

The precipitate (26) is washed until neutral and, after being suspended in water, is decomposed in boiling sol. with hydrogen sulfide, boiled to remove excess of hydrogen sulfide, and filtered. If the filtrate is not clear, the following steps must be taken: the sol. is evaporated to dryness on a water bath, alcohol is added, and the sol. again evaporated. The residue is taken up in hot water and filtered while hot. This treatment generally removes the suspended copper sulfide. If it does not, very dilute nitric acid may be added.

<sup>14</sup> Schreiner and Shorey: Pyrimidine derivatives and purine bases in soils, *Journ. Biol. Chem.*, 1910, viii, p. 385.



The filtrate (27) is allowed to cool, is made ammoniacal, and ammoniacal silver nitrate sol. added until precipitation ceases. If *xanthine* and *hypoxanthine* are present, they will be precipitated as xanthine silver and hypoxanthine silver.

The silver salts are collected on a filter paper and washed with water. The filter and precipitate (28) are placed in an evaporation dish, boiled for a minute with nitric acid sol. (1.1 sp. gr.), filtered hot, washed with the same strength of acid sol. and allowed to cool. Hypoxanthine silver nitrate crystallizes out after several hours and is filtered off.

To the filtrate (29), ammonium hydroxide is added in excess, the precipitate is collected on a filter, washed well with water, and, after suspension in water, is decomposed with hydrogen sulfide, the excess of the latter being removed by boiling, and xanthine identified by its color reactions and characteristic salts.

The precipitate (30) is washed until the washings give a neutral reaction, suspended in water, and decomposed with hydrogen sulfide; excess of hydrogen sulfide is expelled, slight excess of ammonia is added, the sol. warmed to remove the excess of the latter and, after filtering, conc. to small volume. The sol. is then allowed to stand in a cool place, when the hypoxanthine should crystallize out in small colorless needles.

The *second portion* (31) (see page 211) consisting of one-fourth of the original alkaline extract of the soil, is made rather strongly acid with sulfuric acid. The humus precipitate (32) so obtained, after thorough washing, may be added to the humus precipitate from (2) and the filtrate may be shaken out with ether as described in (13) and the ether extract added to (14). After such treatment the filtrate (33) is precipitated with a sol. of phosphotungstic acid and allowed to stand for several days.

The precipitate (34) thus formed is collected on a filter and the filtrate discarded. The precipitate is washed thoroughly with 5 per cent sulfuric acid sol., decomposed by heating with barium hydroxide sol. and the liquid filtered. The filtrate is acidulated with dil. nitric acid and silver nitrate is added until a drop of the sol. added to a saturated sol. of barium hydroxide causes a yellow color to persist. Barium hydroxide is then added to slight alkalinity to precipitate histidine and the sol. is filtered.

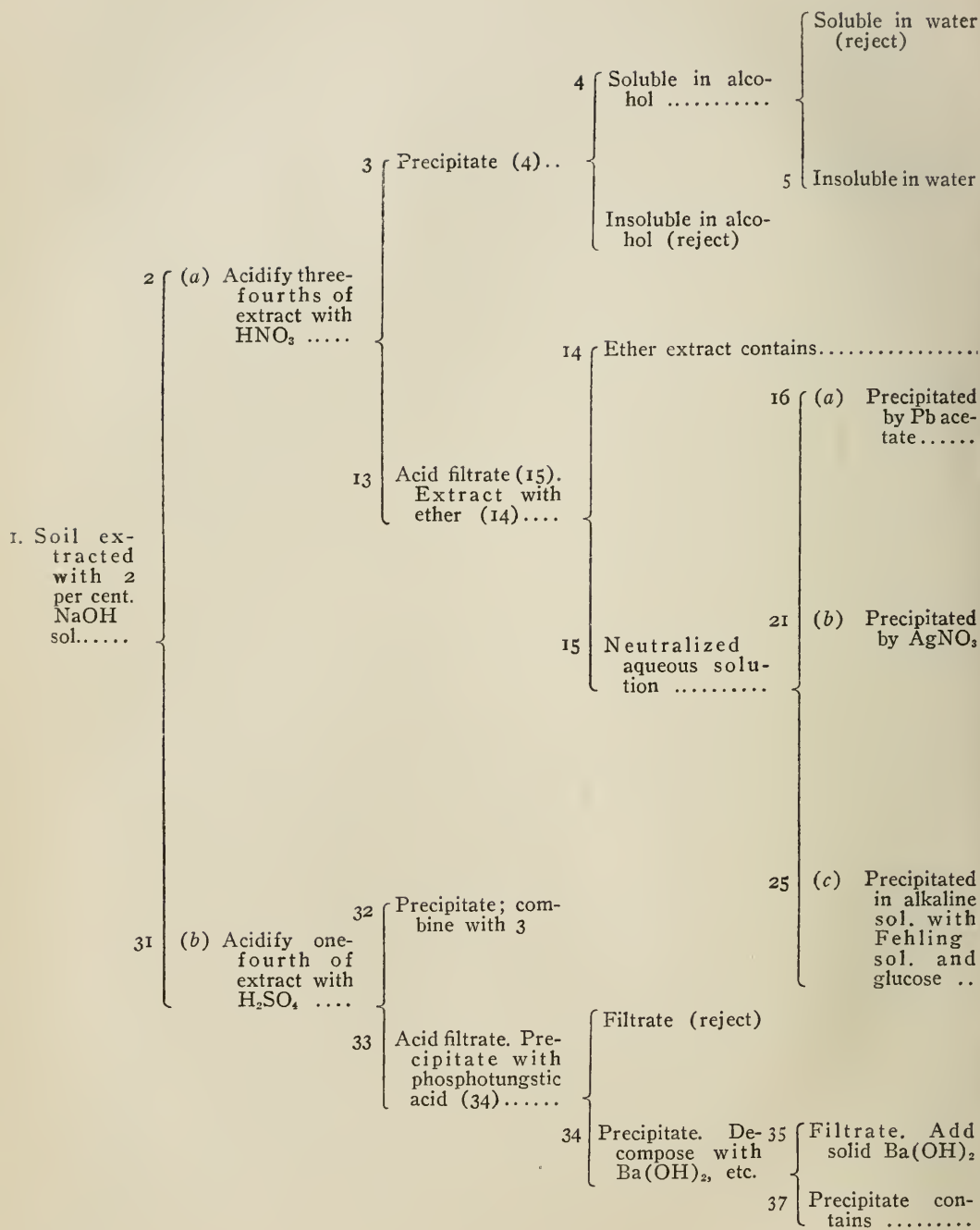
To the filtrate (35) solid barium hydroxide is added to strong alkaline reaction and the precipitate thus formed is collected on a filter paper. If no precipitate is formed, a little more silver nitrate should be added. The precipitate (36) is washed with barium hydroxide sol., suspended in water, acidulated with sulfuric acid, and decomposed with hydrogen sulfide. The sol. is boiled to expel hydrogen sulfide and filtered from the silver sulfide. The filtrate is made slightly alkaline with barium hydroxide (to remove sulfate) and the excess of barium is removed by treatment with carbon dioxide, boiling and filtration. The filtrate is evaporated to a small volume, nitric acid is added and the mixture allowed to stand. Arginine,<sup>15</sup> if present, will crystallize out as arginine nitrate in characteristic form.

*Arginine nitrate* (anhydrous product): m.p., about 175° C., but not sharply; easily soluble in water; easily soluble in hot alcohol, but with difficulty in cold; acid nitrate can be obtained by evaporating the neutral nitrate with excess of nitric acid; crystallizes without water of crystallization in long needles or plates, which melt at 145° C.; free base crystallizes in rosette-like masses or plates melting at 207° C.

The precipitate (37) is washed well with barium hydroxide sol., suspended in water, acidulated with sulfuric acid, decomposed with hydrogen sulfide and the excess of hydrogen sulfide removed by boiling. The sol. is filtered, made alkaline with barium hydroxide (the excess of the latter is precipitated with carbon dioxide), boiled, filtered and evaporated to a small volume. Ammoniacal silver nitrate sol. is added to the filtrate until precipitation is complete, carefully avoiding an excess. The precipitate is collected on a filter, washed well with water, and decomposed with dil. hydrochloric acid sol. After filtering off the silver chloride, the solution is evaporated to a small volume and allowed to stand, when, if present, histidine will crystallize out in the very characteristic form of histidine di-chloride.

*Histidine di-chloride*: m.p., 231° C.; easily soluble in water; crystallizes in characteristic glassy plates or prisms without water of crystallization. The following diazo color reaction of Pauly may be applied: Treat in alkaline sol. with diazo-sulfanilic acid,

<sup>15</sup> Schreiner and Shorey: The presence of arginine and histidine in soils, *Journ. Biol. Chem.*, 1910, viii, p. 381.



*of organic constituents of soils.*

Organic constituents of soils.

6	{	Soluble in petroleum ether	7	{	Insoluble in cold alcohol. Saponify	9	{	Petroleum ether solution contains	{	Hentriacontane	Agrosterol	Phytosterol											
		Soluble in cold alcohol. Precipitate with Pb acetate .....	8	10	{	Residue contains.....	{	$\alpha$ -Mono-hydroxy stearic acid	Lignoceric acid														
				11	{	Precipitate contains.....	Paraffinic acid																
				12	{	Filtrate contains.....	Liquid glycerides																
				{	Insoluble in petroleum ether.....	{	Resin acids	Resin esters															
										Di-hydroxy stearic acid													
17	{	Filtrate. Make alkaline with ammonia....	18	{	Precipitate decomposed with H <sub>2</sub> S; add alcohol	19	{	Precipitate contains.....	Pentosans														
22	{	Filtrate. Make alkaline with ammonia....	23	{	Filtrate (reject)	20	{	Filtrate contains.....	Pentose sugars														
										Picoline carboxylic acid													
										Cytosine													
26	{	Precipitate .. Decompose with H <sub>2</sub> S	27	{	Filtrate. Add ammoniacal silver nitrate.....	28	{	Precipitate. Treat with HNO <sub>3</sub>	29	{	Precipitate contains... Xanthine	30	{	Filtrate contains... Hypoxanthine									
36	{	Precipitate (reject)	30	{	Filtrate (reject)					{	Filtrate contains... Arginine												
										Histidine													

when a red color will be formed which does not disappear on dilution. Tyrosine gives a similar color but the two cannot be confused inasmuch as tyrosine crystallizes in needles that are nearly insoluble in water.

The following concluding statements are quoted from pages 14, 15 and 16 of Bull. No. 80, U. S. Bureau of Soils (see foot-note 3) :

"The amount of a substance obtained may be so small that extreme purification is out of the question, and therefore in such cases, where distinct crystalline form or characteristic tests are not available, the identification becomes uncertain, as neither melting point nor analysis can be made. . . .

"Experience has shown, therefore, that for the best results in searching for a number of compounds not less than 100 pounds of soil should be used, unless the soil be very high in organic matter, or a specific test applied, or the experimenter exceptionally experienced in the isolation.

"The scheme is an adaptation and coördination of the methods of isolating from different soils the single compounds dealt with here. In application of the scheme to different soils it has been found that for each soil some few details in one part or other of the scheme must be more or less modified. This modification is made necessary by the fact that the organic material in different soils is really different, so that the particular compound occurs under different associations, which often render a change in the method of isolation, identification, or purification absolutely necessary. The experience and judgment of the investigator must determine what modification to make. When a substance is isolated and is not identical with the soil constituent already found at this place in the scheme, it may nevertheless belong to the same class of compounds as the constituent already identified. In this manner new compounds may be discovered in the course of such an investigation. Some of the filtrates and precipitates in the scheme are discarded because as yet they have yielded no definite compounds. However, these portions may be examined for such compounds as the investigator sees fit. . . .

"The portions designated for the final isolation and identification of the various compounds will almost always be contaminated with coloring matter, resinous material, and other substances precipitated by the metallic salts or soluble in the same solvents, and such foreign material must, of course, be eliminated by careful reprecipitation or by repeated solution. The metallic salts selected for this investigation as



precipitants do not in most cases completely precipitate the compounds with which they combine, but have been chosen because they seemed to be the most adequate for the purpose. The compounds which they precipitate are often precipitated by other metallic salts used in the scheme; for instance, cytosine, while isolated here by the use of ammoniacal silver nitrate sol., is also precipitated to some extent by ammoniacal lead acetate sol. Care must be taken not to confuse crystals of calcium sulphate with crystals of the hydrochlorides or other salts of the purine bases, for it has been our experience that calcium sulphate often appears in the final solution to be used for the identification of these compounds. Since phosphotungstic acid is a general precipitant for organic bases, some of which may also be precipitated by the other metallic salts used in the isolation of the hexone bases, care must be exercised that salts of other organic bases are not confused with the crystalline salts of arginine or histidine."

The accompanying outline (pp. 218-9), from the Bulletin by Schreiner and Shorey, in 1911 (see foot-note 3 of this paper), will be found very useful in working out the detailed scheme given above.

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## A REVIEW OF RECENT INVESTIGATIONS ON THE MINERAL NUTRITION OF FUNGI

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Pasteur<sup>1</sup> appears to have been the first to make use of a synthetic culture medium for the propagation of lower fungi, and to recognize the importance of mineral nutrients. By means of such a medium he succeeded in demonstrating the differential rate of destruction of the two isomers of a racemic mixture through the action of a common mold. A decade later Raulin<sup>2</sup> proposed a synthetic medium especially adapted to the common black mold, *Aspergillus niger*, with which he carried out his investigations. Raulin's medium is to this day perhaps the best known and most widely used for the cultivation of this and similar organisms. In addition to sucrose and tartaric acid, which supply the necessary carbon, and ammonium nitrate, which furnishes the nitrogen, it contains the following mineral elements: phosphorus, sulphur, potassium, magnesium, zinc, iron and silicon. Raulin showed that the omission of one or more of these elements resulted in a retardation of growth and a decreased yield of the fungus.

By far the greater number of subsequent investigations on the mineral nutrition of fungi have been carried out with this same organism, *Aspergillus niger*. When this fungus is grown upon Raulin's medium at its optimum temperature, 35° C., germination occurs during the first twenty-four hours, the surface of the liquid soon becomes covered with a white mycelium, and about the fourth day black spores appear and the surface of the culture becomes jet black. At room temperature the growth is somewhat slower, the spores making their appearance in about a week. The investigations reviewed below are concerned for the most part with this characteristic organism.

<sup>1</sup> Pasteur: *Compt. rend.*, 51, 298-9 (1860).

<sup>2</sup> Raulin: *Ann. Sci. Nat. (Bot.)*, 11, 93-299 (1869).

The precise rôle of the inorganic nutrients of the medium was not fully understood until comparatively recent years. It is now generally believed that phosphorus and sulphur form an integral part of the fungus, since they go to make up the nucleoproteins and proteins; potassium and magnesium enter into the structural elements of the plant, while iron and zinc act merely as catalysers or stimulants. Until very recently iron was thought to enter into the composition of the coloring matter<sup>3</sup> of the spores, forming a substance analogous to the hematin of the blood of vertebrates. This view has lately been refuted by Javillier and Sauton<sup>4</sup> who showed that iron is not indispensable for the production of the black spores.

The phosphorus assimilation of *Aspergillus niger* has been studied by the writer.<sup>5</sup> Both organic and inorganic compounds of phosphorus, including phytin, glycerophosphate, nucleic acid, lecithin, casein, ovovitellin, and ortho-, pyro- and metaphosphates were available. On the other hand, trivalent forms of phosphorus, such as phosphite and hypophosphite, though not appreciably toxic, could not be utilized as the sole source of this element.

Sulphur likewise forms a great variety of compounds, both organic and inorganic, representing various stages of oxidation. In Raulin's medium the sulphur is supplied entirely in the form of sulphate. As yet, however, very little work appears to have been done on the sulphur assimilation of fungi. Kossowicz and von Groller<sup>6</sup> found that thiosulphate and thiocyanate were available, but the numerous other types of sulphur compounds have not been studied with reference to their availability in culture media. Selenium and tellurium, though presenting many analogies to sulphur, behave quite differently in culture media. Rosenheim<sup>7</sup> introduced compounds of selenium and tellurium into cultures of *Penicillium brevicaulis* and noted the formation of an offensive gas in each case. Although the volatile substances were not identified, they were probably alkyl derivatives of these elements, analogous to the

<sup>3</sup> Linossier: *Compt. rend.*, 112, 489-92 (1891).

<sup>4</sup> Javillier and Sauton: *Ibid.*, 153, 1177-80 (1911).

<sup>5</sup> Dox: *Journ. Biol. Chem.*, 10, 77-80 (1911).

<sup>6</sup> Kossowicz and von Groller: *Z. Gärungsphysiol.*, 2, 59-65 (1912).

<sup>7</sup> Rosenheim: *Proc. Chem. Soc.*, 18, 138-9 (1902).

diethylarsine identified by Gosio<sup>8</sup> when arsenic was added to cultures of this organism.

A number of interesting investigations have lately been carried out with reference to the effect of replacing the inorganic elements of Raulin's medium by other elements in the same group of the periodic system or by elements presenting other analogies.

Potassium is of great importance in the nutrition of fungi. Sauton<sup>9</sup> obtained a yield of 0.165 gm. dry weight of fungus in the absence of potassium, and a yield of 2.6 gm., or nearly 16 times as much, in the presence of 0.003 per cent. of potassium. In the absence of potassium no spores appeared after eight days, but spores soon resulted after addition of this element. Substitution of rubidium and caesium for potassium reduced the dry weight 50 per cent. Assuming that the rubidium and caesium salts used were entirely free from potassium, which may be regarded as somewhat doubtful, it would appear that these elements can replace potassium to a certain extent, though not advantageously. Benecke<sup>10</sup> states that the substitution of rubidium is attended by a diminution in spore production. On account of the decided preference of *Aspergillus niger* for potassium, Sauton<sup>11</sup> suggests this as a method for purifying rubidium and caesium from potassium. Buromsky<sup>12</sup> was unable to obtain normal cultures when the potassium was replaced by sodium. The addition of sodium salts to a potassium free medium gave no better cultures than the control.

Magnesium, like potassium, is indispensable for the normal development of *Aspergillus niger*. Javillier and Sauton<sup>13</sup> find that this element cannot be replaced by glucinum in the culture medium. Frouin<sup>14</sup> used salts of cerium, lanthanum, neodymium, praesodymium, samarium, thorium, and yttrium, and found that none of these elements could take the place of magnesium. Buromsky<sup>15</sup> found that calcium could not replace magnesium. On the contrary,

<sup>8</sup> Gosio: *Rivista d'igiene e sanità pubblica*, 1892, 201.

<sup>9</sup> Sauton: *Compt. rend.*, 155, 1181-3 (1912).

<sup>10</sup> Benecke: *Jahrb. wiss. Bot.*, 37, 487 (1902).

<sup>11</sup> Sauton: *Loc. cit.*, 155, 1181-3 (1912).

<sup>12</sup> Buromsky: *Centrbl. Bakt. II*, 36, 54-66 (1912).

<sup>13</sup> Javillier: *Compt. rend.*, 156, 406-9 (1913).

<sup>14</sup> Frouin: *Compt. rend. soc. biol.*, 73, 640-1 (1912).

<sup>15</sup> Buromsky: *Loc. cit.*

it even had a depressing effect when added to media free from magnesium.

The fact that phosphorus cannot be replaced by arsenic; sulphur by selenium or tellurium; potassium by the other alkali metals; magnesium by glucinum, calcium or the rare earths, indicates that these elements are essential as nutrients.

With the zinc and iron in Raulin's medium the case is quite different. Their function is purely that of a catalyser or stimulant. Javillier and Sauton<sup>16</sup> studied the effect of these two elements on the nutrition of *Aspergillus niger*. In the presence of zinc (0.001 per cent.) and the absence of iron, spores did not appear even after the fourth day. When zinc was absent and iron present (0.001 per cent.) black spores appeared in two days, although the growth was less luxuriant than in the control culture. With both zinc and iron absent, the thin mycelium produced spores as rapidly as in the presence of iron alone. Cultures on zinc and iron together showed a normal amount of growth with spores on the fourth day. Iron is therefore not indispensable for spore formation as had been previously supposed. An interesting observation was the failure of the medium to give the sulphocyanate reaction when both zinc and iron had been omitted. In the absence of zinc, the sucrase<sup>17</sup> of the mycelium was reduced 30 per cent. The enzyme failed to diffuse into the medium or into distilled water, as it does ordinarily. Javillier<sup>18</sup> believes that the zinc regulates the consumption of sucrose, rendering the growth of the plant more economical. This view is held also by Buromsky<sup>19</sup> who finds that zinc increases the respiration coefficient,  $\frac{\text{CO}_2}{\text{weight of fungus}}$ , and diminishes the economic coefficient,  $\frac{\text{sucrose}}{\text{weight of fungus}}$ .

The non-specificity of zinc as a catalyser was established by Lepierre, who succeeded in replacing the zinc of Raulin's medium by a number of other metals. He found, for example, that cadmium<sup>20</sup> can replace zinc and, like the latter, accelerates the growth

<sup>16</sup> Javillier and Sauton: *Compt. rend.*, 153, 1177-80 (1911).

<sup>17</sup> Javillier: *Ibid.*, 154, 383-6 (1912).

<sup>18</sup> Javillier: *Ibid.*, 155, 190-2 (1912).

<sup>19</sup> Buromsky: *Loc. cit.*

<sup>20</sup> Lepierre: *Compt. rend.*, 156, 258-61 (1913).



of *Aspergillus niger*. In concentrations between 0.0002 and 0.002 per cent. the maximum weight of the fungus is obtained. Higher doses than 0.002 per cent. are toxic and the yield diminishes inversely with the concentration. At a concentration of 0.02 per cent. cadmium practically sterilizes the medium. Spore formation is normal at 0.0003 to 0.0002 per cent.; higher doses retard or prevent spore formation, though the maximum yield of the fungus is obtained notwithstanding, and corresponds to that of the zinc medium.

Contrary to the statement of Javillier and Sauton, Lepierre<sup>21</sup> finds that glucinum can replace zinc. The maximum yield is obtained in concentrations between 0.001 and 0.000001 per cent., though the growth is less rapid, requiring nine or ten days. In these concentrations the spore formation is normal. By successive cultures on glucinum the plant acquires a certain degree of adaptation and the response is more rapid.

Likewise uranium<sup>22</sup> can replace zinc as a stimulant, though the same retardation occurs as in the case of glucinum. Concentrations between 0.02 and 0.00001 per cent. give the maximum yield, though not till after ten to twelve days. No growth is obtained at 0.1 per cent. Spores are formed if uranium does not exceed 0.01 per cent.; while at 0.02 per cent. the culture is sterile although it reaches the maximum weight. The action of uranium is, therefore, the same as, but less intense than, that of zinc.

Lepierre<sup>23</sup> finds, further, that copper can replace zinc. Between 0.0002 and 0.0000001 per cent. the yield is normal, but the maximum weight is not attained until after twelve to fifteen days. Above 0.0002 per cent. the yield diminishes, until at 0.2 to 0.1 per cent. there is no growth. Spores appear at the usual time below 0.01 per cent.; below 0.001 per cent. sporulation is delayed twelve to fifteen days.

Lepierre<sup>24</sup> concludes that zinc can not only be replaced by other metals, but can be dispensed with entirely. In the latter case the cultures are luxuriant, but the sporulation is very slow, requiring

<sup>21</sup> Lepierre: *Compt. rend.*, 156, 409-11 (1913).

<sup>22</sup> Lepierre: *Ibid.*, 156, 1179-81 (1913).

<sup>23</sup> Lepierre: *Ibid.*, 156, 1489-91 (1913).

<sup>24</sup> Lepierre: *Ibid.*, 157, 876-9 (1913).

fifteen to twenty days. Zinc is, therefore, useful but not indispensable.

This conclusion of Lepierre regarding the non-specificity of zinc is, however, at variance with the more recent work of Javillier.<sup>25</sup> This investigator maintains that zinc is absolutely necessary for the normal growth of *Aspergillus niger*, but the amount required is so small that it may be obtained by the fungus from the glass culture flask. He finds that a culture in a Jena flask, with or without addition of zinc to the medium, shows a normal growth, whereas cultures in Bohemian glass or quartz vessels give only a fraction of the yield of fungus unless zinc is added. The following is a typical protocoll of Javillier's experiments in this connection.

WEIGHT OF FUNGUS IN GRAMS

	Bohemian	Jena	Quartz
Control .....	0.352	1.861	0.291
With zinc .....	1.780	1.736	1.624

The remarkable effect of minute quantities of manganese was reported by Bertrand.<sup>26</sup> Raulin's medium ordinarily contains traces of manganese as an impurity. Elaborate precautions were taken by Bertrand in purifying the chemicals from manganese before making up the medium. The medium thus prepared did not yield normal cultures, the mycelium remaining sterile. The addition, however, of 0.00001 per cent. of manganese accelerated the growth and increased the yield of the fungus. This extraordinary response to minute quantities of manganese must likewise be regarded as a phenomenon of catalysis.

The absence of calcium from Raulin's medium is quite striking in view of the fact that this element is so necessary for the growth and maintenance of life in animals and higher plants. Robert<sup>27</sup> found that calcium occurs in Raulin's medium as an impurity introduced principally with the sucrose, which may contain as much as 2 mg. of calcium per 100 gm. Using a medium prepared from carefully purified materials free from calcium, he still obtained normal cultures. With the addition of small amounts of calcium, however,

<sup>25</sup> Javillier: *Compt. rend.*, 158, 140-143 (1914).

<sup>26</sup> Bertrand and Javillier: *Ibid.*, 152, 225-8 (1910); Bertrand: *Ibid.*, 154, 381-3, 616-8 (1912).

<sup>27</sup> Robert: *Ibid.*, 153, 1175-7 (1911).

a slight increase was observed in the weight of the fungus, corresponding to the weight of the calcium used. Of 100 mg. of calcium in 250 c.c. of medium, 73.4 mg. of calcium were recovered from the mycelium. Smaller doses were recovered completely. In a later paper Robert<sup>28</sup> showed that the calcium was fixed in the form of oxalate. Analyses of mycelium grown on different amounts of calcium showed calcium and oxalic acid to be present in molecular proportions. This suggests the formations of *raphides* in higher plants, where calcium oxalate may be observed in the form of crystals. Although calcium is fixed by the fungus, its presence is by no means necessary.

There is still a question as to how sharp a distinction can be drawn between nutrients and catalysers. Raulin's medium probably contains other catalysers besides the zinc and iron. The hydrogen ion furnished by the tartaric acid undoubtedly accelerates the growth of the fungus, since the latter does not thrive nearly so well in a neutral synthetic medium. The purpose of adding the acid was originally to aid in sterilization and prevent contamination with bacteria and yeasts, since sterilization of liquids at temperatures above their boiling points was not practised in Raulin's time. Buromsky regards the nitrate ion of Raulin's medium as both catalyser and nutrient. He found the medium to be less efficient when ammonium sulphate was substituted for the nitrate.

Many important problems regarding the mineral nutrition of lower fungi still await investigation.

<sup>28</sup> Robert: *Compt. rend.*, 154, 1308-10 (1912).

## A REVIEW OF WILLSTÄTTER'S RESEARCHES ON CHLOROPHYLL<sup>1</sup>

CLARENCE J. WEST

**Introduction.** Chlorophyll, as is well known, is the green coloring matter in plants and leaves. Accompanying it are two yellow pigments, carotin and xanthophyll.

The history of chlorophyll and its chemical investigation date back to Berzelius,<sup>2</sup> who first attempted to isolate the pigment from leaves. Thinking that it was not affected by conc. hydrochloric acid or alkali sol., he treated the alcoholic extract so vigorously that he obtained only decomposition products. He believed that the green substance was neither a resin, a wax nor a fat but a dyestuff. Since that time much has been published concerning the chemistry of chlorophyll, a great deal of the work being based upon investigations with the spectroscope,<sup>3</sup> but no consistent chemical investigation had been carried out prior to the work of Willstätter and his co-workers.

Chlorophyll is probably present in the leaf in a colloidal form, or as a product of adsorption with colloids, which may be extracted under definite conditions with certain organic solvents because of their dissociating powers. This conclusion is based upon the fact that the spectra of different leaves agree with that of colloidal solutions of pure chlorophyll, though differing in intensity.<sup>4</sup> The idea that chlorophyll is chemically bound in the leaf, with lipoids, for example, is erroneous.<sup>5</sup>

<sup>1</sup> This review is based upon the recent book, *Untersuchungen über Chlorophyll*, by Richard Willstätter and Arthur Stoll; and also upon the numerous articles published by Willstätter in the *Annalen der Chemie*.

<sup>2</sup> Berzelius: *Ann. d. Chem.*, 27, 296 (1839).

<sup>3</sup> References may be found in Marchlewski: *Die Chemie der Chlorophylle* (Braunschweig, 1909).

<sup>4</sup> Herlitzka: *Biochem. Zeit.*, 38, 321 (1912).

<sup>5</sup> Hoppe-Seyler: *Zeit. f. physiol. Chem.*, 3, 339 (1879). Stoklasa: *Ber. d. deutsch. botan. Ges.*, 26, 69 (1907); 27, 10 (1909).

**Chlorophyll of different plants.** Earlier authors supposed that different plants or varieties of plants, such as mono- and dicotyledonous plants, contained different kinds of chlorophyll.<sup>6</sup> Etard<sup>7</sup> claimed that one plant (*Lolium perenne*) contained no less than six different varieties, each fraction of waxy material having been considered a pure chlorophyll. After a careful examination of the chlorophyll from over two hundred different kinds of plants, Willstätter is fully justified in concluding that there is only one chlorophyll,<sup>8</sup> though this exists in two forms. Certain difficulties which were not understood before this conclusion was fully established such as the effect of the enzyme, chlorophyllase, and the effects of the solvent used, the time of extraction, and other conditions, will be considered in detail below.

**Preparation of chlorophyll.** In the preparation of chlorophyll either fresh leaves or dry leaf meal may be used. For the preparation of large quantities of chlorophyll, dry material is preferable, since the yield per kilo is much larger, the leaf containing from 50 to 75 percent of water in the fresh state, depending upon the season. The volume of solvents required is smaller, and the solvents, after being used, are not diluted with the water originally present in the leaf and therefore are more easily recovered. Furthermore, the work may be carried out at any time of the year. The two possible dangers in the use of the dry material are: loss of chlorophyll and chemical changes in the nature of the dyestuff during the process of drying. It has been shown that both of these may be avoided if the drying is carefully carried out. The dry material is used in most of the work described below. In certain cases fresh leaves are preferred—*e. g.*, in the rapid preparation of pure chlorophyll from small amounts of leaves, in the quantitative estimation of the green and yellow pigments, and where the action of chlorophyllase is desired.

The amount of chlorophyll present in one kilo of fresh leaves varies from 0.9 to 2.1 gm. The chlorophyll content of the dry substance varies from 0.5 to 1.0 percent.

<sup>6</sup> Gautier: *Bull. soc. chem.* [4], 5, 319 (1909).

<sup>7</sup> Etard: *La biochimie et les chlorophylles* (1906).

<sup>8</sup> Willstätter, Hocheder and Hug: *Ann. d. Chem.*, 371, 1 (1909); Willstätter and Oppé, *ibid.*, 378, 1 (1910); Willstätter and Isler, *ibid.*, 380, 154 (1911).



Chlorophyll shows certain peculiarities in solubility. Water-free acetone does not extract a trace after standing half an hour, but becomes intensely green upon the addition of a little water. Eighty percent acetone is the most suitable for extraction purposes. Absolute alcohol behaves in the same way, but 90 percent is the most suitable concentration. Ether and benzene become colored only after the addition of a few drops of water. Methyl alcohol is an exception, chlorophyll being nearly insoluble in 80 percent methyl alcohol and readily soluble in the anhydrous solvent. The effect of the water is probably due to the fact that it dissolves some of the mineral salt (potassium nitrate) of the leaf, the resulting salt solution changing the colloidal condition of the chlorophyll in the leaf and rendering it easily soluble.

Three methods of extraction have been used, the last mentioned (below) being the most rapid and giving as pure products as the first two.

The *first* method used was by extraction in a flask. One kilo of leaf meal was shaken with 2 liters of alcohol on a shaking machine for 24 hours, the extract filtered off and the residue washed with alcohol until the filtrate measured 2 liters. This liquid was used to extract a second lot of meal, thus obtaining a so-called double extract.<sup>9</sup>

The *second* method consisted in percolation.<sup>10</sup> In this the meal was moistened with alcohol (0.3 liter per kilo) and allowed to stand three or four hours, sifted and placed in the percolator, care being taken that the material was properly packed, not too tight and without channels. This was then percolated with 2 liters of alcohol per kilo of meal, the operation requiring about 24 hours.

These two methods are open to two objections: The long action of the solvent in contact with the leaf meal is favorable (1) to the action of the chlorophyllase contained in the leaf, which more or less completely decomposes the chlorophyll and (2) it brings about allomerization (see page 235), which is recognized by a change in the decomposition products of the chlorophyll with alkalis.

These objections are overcome or avoided by the *third* method, which consisted in extraction of the pigment on a porcelain funnel

<sup>9</sup> Willstätter: *Ann. d. Chem.*, 350, 65 (1906).

<sup>10</sup> Willstätter and Oppé: *Ibid.*, 378, 5 (1910).

(Nutsche). The leaf meal is placed on the funnel, moistened with the solvent, allowed to stand about five minutes, sucked off and the operation repeated, using for each the same volume of solvent as above, about 1.5 to 2 liters per kilo. The yield of chlorophyll increases with the time of extraction: after 15 minutes, it is 2.9 gm. per kilo; after 2 hours, 4.4 gm.; after 3 days (quantitative estimation), 7.1 gm. The method as actually employed is the following: 2 kilos of dry meal are put on the filter, moistened with 2 liters of 80 percent acetone and then 4 to 4.5 liters added, a liter at a time, with stirring, finally filtering completely from the decolorized meal. This method is better than the one formerly used where 96 percent alcohol was the solvent.

**Purification of chlorophyll extracts.**<sup>11</sup> The chlorophyll extract obtained as above with 80 percent acetone is poured into 4 liters of petroleum ether (d. 0.64–0.66, Kahlbaum), one-half liter of water added and the mixture shaken. The chlorophyll goes into the petroleum ether. After removing the aqueous acetone layer, the petroleum ether is washed twice with 1 liter of 80 percent acetone and the acetone partially removed by washing four times with 500 c.c. of water. All the acetone must not be removed or the chlorophyll will be precipitated. Xanthophyll is then removed by washing the petroleum ether three to five times with 2 liters of 80 percent methyl alcohol. The petroleum ether (now about 3.6 liters) is freed from methyl alcohol and acetone by washing four times with 2 liters of water. During this last washing the petroleum ether loses its fluorescence and becomes turbid because of the precipitation of the chlorophyll. This suspension is shaken with sodium sulfate and 150 gm. of talc, and then filtered through talc. The filtrate still contains a little chlorophyll and most of the carotin. The chlorophyll-containing talc is washed with ordinary petroleum ether, then with low-boiling petroleum ether and finally with one liter of absolute ether, which dissolves out the chlorophyll. This solution is filtered through anhydrous sodium sulfate, conc. to 25 c.c., and precipitated by pouring into 0.8 liter of low-boiling petroleum ether. The yield is about 13 gm., or 6.5 gm. per kilo of leaf meal. The yield is about 0.75 percent of the content of the dry leaf and the chlorophyll has a purity of about 98 percent.

<sup>11</sup> Willstätter and Hug: *Ann. d. Chem.*, **380**, 177 (1911).

Chlorophyll with a purity of about 95 percent, so-called "roh-chlorophyll," is more easily obtained as follows: 2 kilos of meal are extracted (as above) with 6 liters of 78 percent acetone for 30-40 minutes, giving 4 liters of extract. This is diluted with one-fourth to one-half of its volume with 80 percent acetone, and the chlorophyll precipitated by the gradual addition of 1.2 liter of water. The suspension is shaken with 300 to 400 gm. of talc, filtered, washed with 2 or 3 liters of 65 percent acetone, the chlorophyll extracted with ether, the ether evaporated to a syrupy consistency and mixed with 1.5 to 2 liters of petroleum ether. The yield is from 12 to 14 gm., and the purity about 95 percent, as mentioned above.

The preparation from *fresh* leaves is practically the same as given above, except that pure acetone is used for the extraction, the water content of the leaves diluting it to such an extent that two extractions remove practically all the chlorophyll.

**Properties of chlorophyll.**<sup>12</sup> Pure chlorophyll conforms to the following standards:

1. The ash content is 4.5 percent; the ash is pure magnesium oxide. (The statements of Stoklasa concerning the phosphorus and potassium content of the ash are not correct.)

2. The phytol content of the chlorophyll is one third of the molecule; the phytol is free from solid admixtures.

3. The chlorophyll does not contain yellow pigments.

4. When saponified with alkali (an ether sol. is shaken with methyl alcoholic potash sol.) the color changes to a pure brown. Mixtures give a dirty brown; the allomerised product does not give the test.

5. Decomposition, by boiling with alcoholic potash, yields the normal mixture of phytochlorine *e* and phytorhodine *g*.

6. The spectrum agrees with that of a fresh leaf extract.

Chlorophyll is a bluish black substance with a strong, nearly metallic luster. When dry, it may be easily pulverized to a greenish or bluish black powder. It does not possess a definite melting point, 93°-96° and 103°-106° being found for two samples. It is soluble in absolute alcohol with a bluish green color. It is quite insoluble in cold petroleum ether, but becomes easily soluble after the addi-

<sup>12</sup> Willstätter and Hug: *Ann. d. Chem.*, 380, 204 (1911).

tion of a little methyl or ethyl alcohol. It shows neither acid nor basic properties. By the action of acids the color is changed into olive brown, the magnesium being split off. Picric acid does not give a picrate but decomposes the chlorophyll, giving a brown solution.

**Chlorophyll a and b.** Chlorophyll, as ordinarily obtained, is a mixture of two components, designated as *a* and *b*. This fact was first noticed by Stokes,<sup>13</sup> who used alcohol and carbon disulfide to "disentangle the two." The method now used depends upon the partition of the chlorophyll mixture between methyl alcohol and petroleum ether; component *a* goes into the petroleum ether, component *b* into the methyl alcohol phase. The method is carried out as follows:<sup>14</sup> Eight grams of chlorophyll are dissolved in 150–200 c.c. of ether, filtered and poured into 4 liters of petroleum ether, 50 or 100 c.c. of methyl alcohol being added if necessary to clear the solution. This liquid is then extracted fourteen times with 2 liters of 85 percent methyl alcohol, previously saturated with petroleum ether and containing 0.01 gm. of oxalic acid per liter. This removes practically all of component *b*. The methyl-alcohol extracts are brought to a concentration of 90 percent, washed with 1 liter of petroleum ether, poured into 2 liters of ether and mixed with a large quantity of water. The ether-petroleum ether sol. is then freed from methyl alcohol by washing with water, conc. to 500 c.c. and then in vacuum to 30–40 c.c., and chlorophyll *b* precipitated with 300 c.c. of petroleum ether (boiling between 30° and 50° C.) and the precipitation repeated twice, when it is free from component *a*. The petroleum ether sol. of *a* is washed with water until all the chlorophyll is precipitated, the suspension filtered, the chlorophyll taken up in ether and the ether removed in vacuum. The yield of *a* is about 3.5 to 4 gm., of *b*, about 1.5 gm., together with 2 or 3 gm. of a mixed chlorophyll.

**PROPERTIES OF CHLOROPHYLL *a* AND *b*.** Chlorophyll *a* is characterized by giving a pure yellow phase with methyl alcoholic potash sol. and only phytychlorine *e* as a decomposition product. It crystallizes in thin lancet-like leaflets forming a bluish black powder with steel blue luster. It melts at 117°–120° C. The ethyl

<sup>13</sup> Stokes: *Proc. Royal Soc.*, 13, 144 (1864).

<sup>14</sup> Willstätter and Isler: *Ann. d. Chem.*, 390, 269 (1912).



alcohol sol. is bluish green with a deep red fluorescence. It is insoluble in 80 percent methyl alcohol and in petroleum ether. The ethereal sol., shaken with 6 percent hydrochloric acid, is slowly decomposed, while 20 percent acid decomposes it immediately.

Chlorophyll *b* gives a dark red phase with alkali, and as a decomposition product only phytorhodine *g*. It is dark green to bluish black in color; usually forms crystals that may easily be filtered off; and, in general, is less soluble than the *a* component, being entirely insoluble in cold petroleum ether. The alcoholic sol. has a yellowish tinge when compared with that of *a*. It fluoresces brownish red. A colloidal solution is yellow green with a dark olive green opalescence. It is somewhat less easily decomposed by shaking with acids.

There seems to be a fairly definite relation between the two components, one molecule of chlorophyll *b* being accompanied by three molecules of chlorophyll *a*. (In the same way a similar relation is found between the yellow pigments, one molecule of carotin being accompanied by about one and a half molecules of xanthophyll. The relation between the chlorophyll (*a* + *b*) and the yellow pigments is about one molecule to 0.35 molecule.)

The analyses of the two components, dried in a high vacuum, interpreted in the light of analyses of decomposition products of these substances, lead to the following formulas:

Chlorophyll *a*:  $C_{55}H_{72}O_5N_4Mg + 0.5 \text{ mol. of } H_2O \text{ (half hydrate).}$

Chlorophyll *b*:  $C_{55}H_{70}O_6N_4Mg.$

Several of the compounds studied give analytical figures for 5.5 or 6.5 atoms of O. Since molecular weight estimations indicate that the molecule is not to be doubled, these compounds are to be considered as half hydrates.

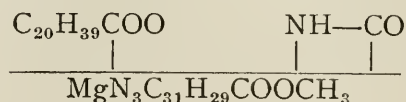
**Allomerization.**<sup>15</sup> It was mentioned above that allomerization was one of the difficulties met with in the earlier methods of extraction. This name is given to a certain change, perhaps isomeric in nature, which chlorophyll and some of its decomposition products undergo when allowed to stand in alcohol or petroleum ether sol. for some time. The allomerized product has lost its property of

<sup>15</sup> Willstätter and Utzinger: *Ann. d. Chem.*, **382**, 129 (1911); Willstätter and Stoll: *Ibid.*, **387**, 317 (1911).

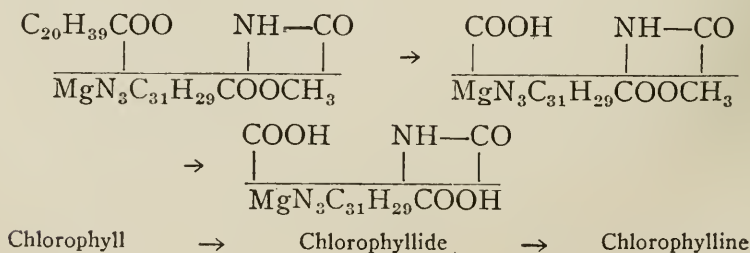


crystallizing, its ether solution does not give the brown phase when shaken with alcoholic potash sol., and it does not yield the normal decomposition products but more weakly basic ones. It is thought that the change consists in the opening of the lactam group and the formation of a new lactam group (see page 243). If a different amino group or carboxyl group is involved in this reaction it is clear that an isomeric chlorophyll of different basic or acidic character will be formed. Allomerization does not take place in ether, chloroform or water-free pyridine. It appears to be catalysed by glass, since an alcoholic sol. in a platinum or silver vessel shows very little change. While it does not appear that the alkali of the glass is responsible for the change, yet it is completely prevented by the presence of small amounts of acid, 0.01 gram of oxalic acid in 1 liter of alcohol being sufficient. This accounts for the presence of oxalic acid in the alcohol used for the separation of the two chlorophyll components.

**The chemical properties of chlorophyll.** The parent substance of chlorophyll is a tricarboxylic acid, called chlorophylline,  $C_{31}H_{29}N_4Mg(CO_2H)_3$ . In chlorophyll one carboxyl group is esterified with methyl alcohol, a second with the unsaturated alcohol, phytol,  $C_{20}H_{40}O$ , while the third is probably present as the lactam group. Thus we may represent chlorophyll, or methyl phytol chlorophylline, in the following manner :

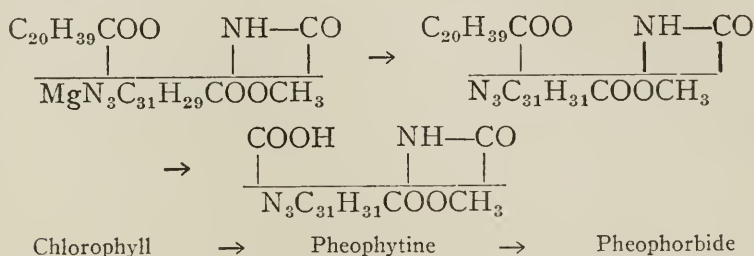


When treated with the enzyme, the phytol group is split off, giving *chlorophyllide*, or methyl chlorophylline, which loses its methyl alcohol group under the influence of hot or cold alkali sol., giving chlorophylline :



At higher temperatures the alkali causes decompositions, with the elimination of carbon dioxide and the formation of the phylines and porphyrines.

Gentle treatment with acids first causes a displacement of the magnesium by two atoms of hydrogen, forming pheophytine; more vigorous treatment saponifies the phytol group with the formation of pheophorbide:



**Chlorophyllase.**<sup>16</sup> The second objection to the earlier methods of extraction was the action of the enzyme. It was found early in the work on chlorophyll<sup>17</sup> that the preparations varied greatly in their phytol content, especially if the extract was allowed to stand in contact with the leaf meal for any length of time. At first this was thought to be due to differences in the chlorophylls of different plants, but later it was found that the green plant contained an enzyme which had the property of splitting phytol from chlorophyll. This enzyme has been called chlorophyllase. It is especially stable, as its use in conc. alcohol and acetone sol. shows, even withstanding short heating in alcoholic sol. It is destroyed by treating the leaves with boiling water. It is insoluble in organic solvents, as the extracts, after being filtered from the leaf meal, are not further changed. Chlorophyllase has been found in all the classes of plants investigated, though only in a few in sufficient quantity for preparative purposes: hemp nettle, hogweed and hedge nettle.

Chlorophyllase is used in the form of the dry leaf meal, ground, and usually extracted with alcohol to remove most of the chlorophyll. The strength of the enzyme is measured as follows: If one kilo of dry leaf meal yields an extract of 3 gm. of chlorophyll and contains

<sup>16</sup> Willstätter and Stoll: *Ann. d. Chem.*, 378, 18 (1910); 380, 154 (1911); 387, 317 (1911).

<sup>17</sup> Willstätter and Oppé: *Ibid.*, 378, 4 (1911).

in all 5 gm. of the pigment, then 60 gm. of this dry material is said to be an  $n/10$  enzyme; that is, 0.1 of the material which would contain 3 gm. of chlorophyll. The course of the reaction may be followed by estimating the amount of free chlorophyllide colorimetrically after extraction with  $n/50$  potassium hydroxide sol., by determining the phytol number, or by splitting off the methyl and ethyl groups with hydroiodic acid according to Zeisel.

Since the enzyme is used in the form of a powder, the reaction proceeds faster when the suspension is stirred. An attempt to apply the law for monomolecular reactions to the enzyme in alcoholic solution, using the formula

$$K = \frac{1}{t} l_n \frac{a}{a - u},$$

gave values for  $k$  which decreased considerably as the reaction proceeded.

*N/10 enzyme at 25° C., 500 c.c. of extract containing 1.8 gm. of chlorophyll.*

Time in hours	$Z_u$	$u$	$k \cdot 10^3$
10	25.6	24.0	27.5
20	23.2	33.1	20.0
40	19.1	47.1	15.9
80	12.0	69.0	14.7

This may be due to a co-enzyme or activator, which decreases the rate of reaction; or it may be that during the action the enzyme is gradually destroyed or its activity decreased. This is seen in the following experiments.

The enzyme was allowed to act on chlorophyll for periods of two and one-half, five and ten hours, and then was used for fresh solutions of chlorophyll. The results are given in the appended table:

	Time in hours	$u$	$k \cdot 10^3$
Experiment I.....	2.5	23.8	108.7
" II.....	5	34.8	85.4
" III.....	10	54.7	79.1
Enzyme, Exp't. I.....	2.5	24.2	110.7
" " II.....	5	19.2	85.4
" " III.....	10	15.7	68.3

Double amounts of enzyme produced the same effect in five hours that half that amount produced in ten hours. Thus the action followed Schütz's law:  $u = k \sqrt{Et}$ . This law also held for values in the ratio of 1:2:4. Decreasing the concentration of the chlorophyll sol. decreased the value of  $k$ .

The presence of water is favorable to the reaction; 92 percent alcohol gave a value of 57.4 for  $k$ , while under the same conditions 80 percent alcohol gave a value of 140.3. Calcium carbonate is without effect upon the enzyme; magnesium oxide retards its action very markedly.

The optimum temperature for the action of chlorophyllase is 20°, the value for  $u$  after five hours being 33.3; at 25°,  $u$  is 25.3; at 35°, 21.9. Heated two days at 50° the meal was nearly enzyme-free. Treated for forty minutes with boiling 96 percent alcohol, the enzyme still retained about 0.2 of its original power.

Some of the enzyme may be pressed out with the juice of the leaf, though the press cake is more active than the extract. The enzyme in the juice may be precipitated by adding two vol. of absolute alcohol.

The following reactions may be carried out by the use of chlorophyllase:

Chlorophyllase, acting upon an ethyl alcohol sol. of chlorophyll, saponifies off the phytol group and esterifies the free carboxyl group thus formed with ethyl alcohol. This gives ethyl chlorophyllide, which is the crystalline chlorophyll of Borodin. If methyl alcohol is used, methyl chlorophyllide is formed in the same way. If, however, the action is carried out in moist acetone or ether, the phytol group is hydrolyzed off and the free carboxyl group results, thus giving chlorophyllide.

The reverse reaction may also be carried out. When free chlorophyllide  $a$  and phytol were mixed and allowed to stand 24 hours with meal of leaves rich in chlorophyllase, it was found that at least 20 percent of the chlorophyllide had been converted into chlorophyll  $a$ . If a little water is present the amount of chlorophyll formed corresponds to 60 percent of the chlorophyllide, while 65 percent seems to be the point of equilibrium.

**Crystalline chlorophyll.**<sup>18</sup> Borodin<sup>19</sup> in 1881 obtained a

<sup>18</sup> Willstätter and Benz: *Ann. d. Chem.*, 358, 267 (1907).

<sup>19</sup> Borodin: *Bot. Zeitung*, 40, 608 (1882).

crystalline form of chlorophyll. Monteverde,<sup>20</sup> observing the same in 1893, considered it pure chlorophyll, regarding the amorphous form as the decomposition product of the crystalline form. The true relation was first shown by Willstätter. As mentioned above, amorphous chlorophyll is changed into the crystalline form by replacing the phytyl group with an ethyl or methyl group, and while amorphous chlorophyll is phytyl chlorophyllide, crystalline chlorophyll is ethyl or methyl chlorophyllide.

The preparation of crystalline chlorophyll is carried out as follows: The dry meal is allowed to stand with 90 percent alcohol for 12 hours (2 liters of alcohol for 1 kilo of leaf meal), the meal filtered off with suction and washed with 2.5 liters of acetone, which dissolves out the crystalline chlorophyll that remains in the leaf cells. The two extracts are combined, shaken with 150 gm. of talc and during the course of an hour diluted with 4.5 liters of water. The chlorophyllide separates in large glistening crystals, which are filtered off with the talc, washed with 55 percent acetone and alcohol, then with petroleum ether and ether, taken up in alcohol, poured into ether, the alcohol washed out with water and the ether dried. After conc., the chlorophyllide crystallizes as three-sided tables.

**Decomposition products of chlorophyll.** The decomposition products of chlorophyll *a* and *b* are shown in the table on page 241. From this table may also be seen the relations between the successive stages in the degradation of the complex molecule, which may be brought about by the consecutive application of acid and alkaline hydrolyses. These relations will be indicated more fully in the discussion of the various substances named in the table. In the majority of cases it has been found easier to carry out the reaction on the chlorophyll mixture and then separate the new mixture into its components.

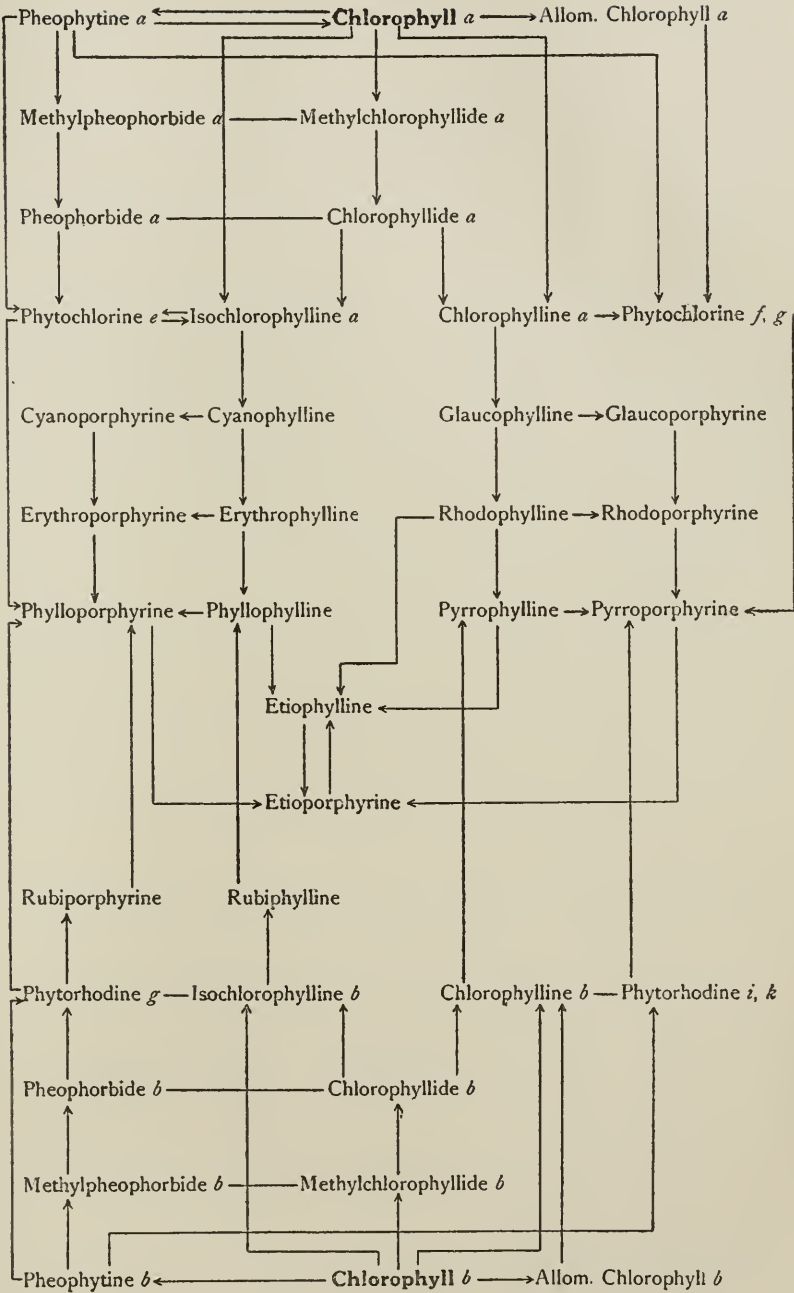
**DECOMPOSITION WITH CHLOROPHYLLASE.** Chlorophyllase, acting upon chlorophyll in methyl alcohol sol. or, better, in a solution made up of 78 parts of acetone, 15 parts of methyl alcohol and 7 parts of water, for 40 hours, splits off the phytol residue and replaces it by a methyl group, forming *methyl chlorophyllide*,<sup>21</sup>



<sup>20</sup> Monteverde: *Acta Horti Petropolitani*, 13, 123 (1893).

<sup>21</sup> Willstätter and Stoll: *Ann. d. Chem.*, 387, 351, 355 (1912).





which may be separated into its components by shaking the ether-petroleum ether sol. with 60 percent methyl alcohol, thus removing the *b* component. Component *a* is bluish black, giving a bluish green or green sol. One gram dissolves in 760 c.c. of ether, giving a sol. easily decomposed by 10 percent acid. Component *b* is greenish black and gives a yellowish green or green sol. One gram dissolves in 2.8 liters of ether and is decomposed by 15 percent acid. It does not react with ammonia gas.

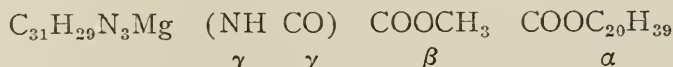
Chlorophyllase, acting upon chlorophyll in moist ether or dilute acetone, gives *chlorophyllide*,  $C_{32}H_{30}ON_4Mg(COOH)(COOCH_2)$ , the two components of which may be separated by the use of 50 percent methyl alcohol. It may also be obtained from the methyl derivative but the reaction is much slower than in the case of chlorophyll. The enzyme appears to be fairly specific for chlorophyll, for in the case of pheophytin the reaction is also very slow. The *a* form crystallizes with half a molecule of water, as green or bluish green six sided tables, while the *b* form is yellow to olive green. The free carboxyl group gives it marked acid properties, *a* being extracted from ether with  $n/1000$  potassium hydroxide sol., while *b* is nearly quantitatively extracted by  $n/2000$  potassium hydroxide sol. It is quickly allomerized in alcoholic sol. With dry ammonia gas it gives a precipitate of an ammonium salt which may be decomposed by shaking with moist ether. Upon warming in vacuum, or upon standing in dilute sol., it decomposes forming magnesium pheophorbide.

DECOMPOSITION WITH ALKALI. Chlorophyll, reacting with methyl alcoholic potassium hydroxide sol., gives rise to two products depending upon the conditions used: chlorophylline and isochlorophylline, which are unstable tricarboxylic acids and have been studied in the form of their salts. If the saponification is carried out in the cold with conc. methyl alcoholic potash sol., the principal product of the reaction is chlorophylline potassium *a*; either the extract or the purified chlorophyll may be used, a much purer product being obtained from the purified chlorophyll. If allomerized chlorophyll is used, this is the only product formed. The pure cryst. potassium salt may be easily obtained by shaking a petroleum ether sol. of 3 gm. of chlorophyll *a* with 10 cc. of 7 percent methyl alcoholic potash sol. The salt crystallizes in dark blue leaflets. It is characterized

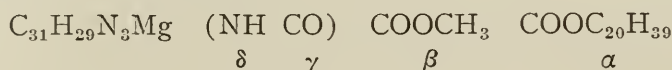
by the fact that upon further decomposition it gives phytochlorine *f* and *g*, which are less basic than the normal decomposition products.<sup>22</sup>

If on the other hand, a hot alcoholic potash sol. is used, 1 gm. of methyl chlorophyllide being heated five minutes to gentle boiling with 25 c.c. of conc. potash, then 2 or 3 c.c. of water added and the mixture heated a few minutes longer, there results isochlorophylline, the potassium salt of which is dark blue, and gives solutions which fluoresce, while those of the chlorophylline salts do not. This gives the normal phytochlorine *e* upon treatment with acid.<sup>22</sup>

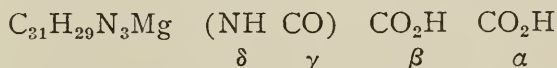
Willstätter has attempted to explain these reactions by means of the lactam rearrangement, that is, the opening of a lactam ring already present in the molecule and the formation of a new, similar, but alkali-stable, ring. In chlorophyll he supposes the following groupings:



If, under the influence of alkali, the lactam ring were opened, the carboxyl group thus formed would be free to unite with the same or another amino group present in the molecule, such as  $\delta$ . This would give a new compound:



If, in this process, the esters were saponified, there would result a compound to which Willstätter has given the name chlorophylline:



It is also possible that, after the lactam group is opened and the  $\alpha$ -carboxyl group is freed by saponification, this would react with the freed amino group, which would then give the isomeric compound, called iso-chlorophylline:



<sup>22</sup> Willstätter: *Ann. d. Chem.*, 350, 48 (1906); Willstätter and Utzinger: *Ibid.*, 382, 129 (1911).

The allomerized product probably has the same structure as the product obtained by the action of alkali in the cold, *i. e.*, the original lactam group may be opened by the continued action of alcohol or petroleum ether; and since the new group is not reactive, the reaction proceeds to completion in the direction of the allomerized product. It is also possible that the original lactam group may be opened in alkaline sol. and then reformed again. This possibility is found in the "brown-phase" test. If an ethereal sol. of chlorophyll is shaken with methyl alcoholic potash sol., the chlorophyll goes quantitatively into the alkaline layer with a brown color. If this is now shaken with water, the salt is dissociated and the chlorophyll is found unchanged in the ether. It will again respond to the "brown-phase" test. The allomerized product does not give the "brown-phase" test, for a new and more stable lactam grouping is formed in the process of allomerization.

DECOMPOSITION WITH ACIDS. The action of acids, upon chlorophyll and the magnesium-containing derivatives obtained by the action of alkali, consists in the quantitative removal of the complexly bound magnesium and the substitution of two atoms of hydrogen. The resulting products are free from mineral constituents. By the mild action of acids the two ester groups of chlorophyll are not affected. In this reaction the color changes from green to brown; the resulting products are much more insoluble than are the mother substances and this furnishes a convenient method for estimating chlorophyll derivatives: first, because of the greater insolubility of the products and second, because these compounds are not as easily allomerized.

The preparation of *pheophytin*<sup>23</sup> is best carried out by using a 90 percent alcoholic extract of chlorophyll, which is shaken with a conc. oxalic acid sol. or alcoholic hydrochloric acid at room temperature. Four kilos of dry leaf meal are extracted with 6 liters of 90 percent alcohol, giving 4 liters of extract, the process taking about 20 minutes. The extract is filtered and the filtrate from two extractions united and treated with 160 c.c. of 10 percent alcoholic hydrochloric acid. After standing an hour the pheophytin has almost completely precipitated out. The mother liquor is decanted and the precipitate filtered off, giving from 28 to 40 gm. of almost

<sup>23</sup> Willstätter and Hocheder: *Ann. d. Chem.*, 354, 218 (1907).

pure pheophytin. By means of this process a laboratory worker is able to work up 40 to 48 kilos of leaf meal a day, giving 200 to 250 gm. of pheophytin. When saponified it gives a mixture of phytochlorine and phytorhodine. It is very slightly basic, not being extracted from its ether solution with 25 percent hydrochloric acid. It has no acid properties. It is waxy in nature and has not been obtained in good crystalline form. It reacts with metallic salts to form colored and very stable complexes. Thus, iron salts give a greenish blue solution; zinc acetate, bluish green; copper acetate, brown solutions which become green on dilution. When heated with magnesium oxide and methyl alcoholic potash sol., magnesium is introduced into the molecule, but under the influence of the strong hot alkali, the chlorophyll which might result is decomposed. However, if the Grignard reagent is used, pure chlorophyll *a* may be obtained from pheophytin *a*.

Pheophytin *a* is best prepared by extracting it from a mixture of the two components with 30 percent hydrochloric acid. This separation must be carried out in the cold and as rapidly as possible for the substance is quite easily hydrolyzed.

The hydrolysis of pheophytin cannot be carried out with chlorophyllase because the reaction is too slow. It is brought about by heating with alcoholic hydrochloric acid for one hour, during which the phytol group is saponified off and replaced by a methyl group. The mixture of *methyl pheophorbide a* and *b* is fractionated by means of 17 percent hydrochloric acid, the *a* form being removed.<sup>24</sup>

The methyl group may be removed by dissolving the ester in ether (2 gm. in 4 liters) and extracting three times with one-half a liter of 25 percent hydrochloric acid. The acid sol. is allowed to stand at room temperature for two hours, when the saponification is complete. The free pheophorbide is also obtained by the hydrolysis of pheophytin; 4 gm. of pheophytin are dissolved in 800 c.c. of ether and 2 liters of hydrochloric acid, and allowed to stand from three-fourths to one hour, when the acid sol. is diluted and extracted with 7 liters of ether. The components may be separated by extracting *a*, using five portions of 1 liter each of 16 percent hydrochloric acid. It may also be extracted with  $n/100$  ammonia or potassium hydroxide sol., 0.1 percent sodium carbonate or 1

<sup>24</sup> Willstätter: *Ann. d. Chem.*, 387, 370 (1912).



percent sodium bicarbonate sol. Disodium phosphate precipitates the pheophorbide quantitatively. It is more stable than the corresponding chlorophyllide.

In the same way that chlorophyll gives pheophytine, methyl chlorophyllide and chlorophyllide give methyl pheophorbide or pheophorbide with mineral acids or oxalic acid.

**Phytochlorine; phytorhodine.**<sup>25</sup> Phytochlorine *e* and phytorhodine *g* are the most important products of the hydrolysis of pheophytine and the other pheophorbides. Each is obtained, however, not simply by the saponification of the two ester groups but simultaneously by one of several possible rearrangements of the lactam groups and is therefore dependent upon the conditions of hydrolysis. These conditions vary, depending upon whether the purpose of the experiment is the isolation of phytol or of the basic decomposition products. It may be carried out with hot or cold alcoholic potash sol., but never with any other solvent.

Three methods have been used for this reaction. The *first* consists in heating 1 gm. of pheophytine with about 6 c.c. of methyl alcoholic potash sol. (200 gm. of potassium hydroxide in 1 liter of methyl alcohol). One hundred grams may be worked up in one portion. The period of heating depends upon the state of division, a fine powder requiring not more than half an hour; the time involved does not affect the production or purity of the phytol but does affect the basic part of the molecule, the longer the heating the larger the yield of amorphous, insoluble material.<sup>26</sup> For the preparation of phytol the reaction product is diluted with water and extracted with ether.

The *second* method consists of saponification in the cold. One gm. of pheophytin is shaken with from 6–10 c.c. of 40 percent methyl alcoholic potash sol. for two or three days at room temperature; or 1 gm. of the alkyl pheophorbide for two hours with ten parts of potash sol. containing 10 percent of water. The phytol is extracted as explained above.

The *best method* for preparing phytochlorine *e* consists in dissolving pheophytin in 20 c.c. of pyridine at 80°, pouring into an alkaline sol. of 250 c.c. of methyl alcohol and 160 gm. of potassium

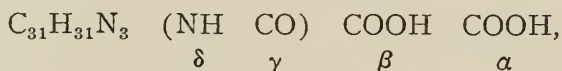
<sup>25</sup> Willstätter: *Ann. d. Chem.*, 354, 205 (1907); 382, 129 (1911).

<sup>26</sup> Willstätter: *Ibid.*, 380, 162 (1911); 382, 189 (1912).

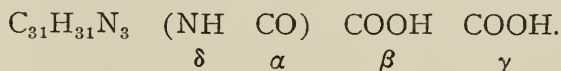
hydroxide, heating to boiling half a minute and cooling quickly. In order to separate the phytochlorine from the phytorhodine, the phytol is first extracted with ether; the product is then covered with ether and acidified with 20 percent hydrochloric acid, which causes the basic portion to go into the ether layer. The ether is then shaken eight times with 1 liter of 3 percent hydrochloric acid in order to extract the phytochlorine, neutralized with ammonia and taken up in ether. The last trace of phytochlorine is removed from the ether by shaking with 5 percent acid. Phytorhodine is extracted by shaking with 9 percent acid.

As may be seen from the table (page 241), isochlorophylline *a*, obtained by the saponification of chlorophyll and the chlorophyllides with hot alkali, is the magnesium-containing derivative that corresponds to phytochlorine *e*, and upon acidification gives phytochlorine *e* in a high state of purity. This method of preparation is not convenient, however, because the preparation of isochlorophylline is difficult, and unless it is saponified under exact conditions, less basic products result. The reaction may be carried out by allowing barium hydroxide to react with a crude-chlorophyll sol. and then acidifying the barium salt.<sup>27</sup>

In the same way phytochlorine *f* and *g* result from chlorophylline. From the formulas given above for the chlorophyllines, we may write the following for phytochlorine *e*,



and for phytochlorine *f* and *g*,



Phytochlorine *e* exists in two modifications, a lactam hydrate of the formula,  $\text{C}_{34}\text{H}_{36}\text{O}_6\text{N}_4$ : thick leaflets with a violet luster; and as the lactam of the formula,  $\text{C}_{34}\text{H}_{34}\text{O}_5\text{N}_4$ : rectangular tables. Both forms give brownish black powders. The hydrate form is stable when dried, while the anhydrous form gradually changes. They have different solubilities. The solution in conc. sulfuric acid is

<sup>27</sup> Willstätter and Utzinger: *Ann. d. Chem.*, **382**, 162 (1911).

bluish green, in conc. nitric acid, emerald green. Both modifications show strongly acid properties, being completely extracted from ether by 0.01 percent ammonia. It forms a characteristic tri-potassium salt—brown or steel blue prisms; a cesium salt (complex salt)—steel-blue prisms: and a trimethyl ester—long, steel-blue prisms, melting at  $188-90^{\circ}$ , which may be hydrolyzed with alcoholic potash.

Phytochlorine *f* has been isolated in a pure state and is isomeric with the anhydrous form of phytochlorine *c*. This is extracted from ether by 11 percent hydrochloric acid.

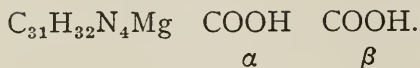
Phytorhodine *g*,  $C_{34}H_{34}O_7N_4$ , crystallizes from ether in large six-sided prisms, having a dark red color with metallic luster. It may be extracted from ether with 0.001 percent ammonia. Its trimethyl ester forms black, rectangular tables, melting at  $207^{\circ}-210^{\circ}$ .

**The phyllines and porphyrines.**<sup>28</sup> The magnesium complex of the chlorophyll molecule remains intact when heated with alkali and a series of magnesium-containing carboxylic acids result, having splendid blue and red colors. These are called phyllines. A second series of acids is obtained by removing the metal with mineral acids, giving the so-called porphyrines. Isochlorophylline *a* gives, under these conditions—the dicarboxylic acids: cyanophylline, in solution blue; and erythrophylline: in solution red; the monocarboxylic acid: phyllophylline, in solution bluish red. Chlorophylline *a* gives the dicarboxylic acids: glaucophylline, in solution blue; and rhodophylline, bluish red; and the monocarboxylic acid: pyrrophylline, in solution bluish red. The *b* series is decomposed with more difficulty, because it contains an extra oxygen atom, which must be reduced without splitting off carbon dioxide. This has been accomplished by the use of pyridine. The end products are the same, namely, phyllophylline and pyrrophylline. Of the dicarboxylic acids, only rubiphylline has been isolated in a pure state.

The first change or decomposition of the chlorophylline molecule is brought about by heating with methyl alcoholic potash six and one half hours at  $140^{\circ}$ , the reaction being smoother if pyridine is added to the reaction mixture. In this the lactam group is broken open and probably the carboxyl group thus formed is split off as

<sup>28</sup> Willstätter and Pfannenstiel: *Ann. d. Chem.*, 358, 267 (1907); Willstätter and Fritzsche: *Ibid.*, 371, 33 (1909).

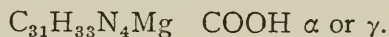
carbon dioxide. Chlorophylline gives *glaucophylline*, which may be represented as



The reaction product is precipitated by diluting with water, the moist salt covered with one part of alcohol and six parts of ether, and the suspension acidified with conc. monophosphate sol. The free *glaucophylline* goes into the alcohol-ether mixture, the alcohol is washed out with water, which causes a precipitation of impurities and gives a blue color to the *phylline* sol., and a bluish red fluorescence. The solution is further purified by shaking with 0.004 percent ammonia five or six times, which extracts the *phylline*. Acidified with a little primary phosphate, it is again brought into ether, which is then shaken with a little very dilute disodium phosphate sol. Upon concentrating the sol., the *phylline* precipitates as small prisms having a blue surface luster.

Under the same conditions *isochlorophylline* gives *cyanophylline*,<sup>29</sup> in which the carboxyl groups  $\gamma$  and  $\beta$  are probably present. This substance is very unstable and, upon standing, the fresh solution quickly becomes turbid, because of the splitting out of the magnesium.

If the temperature is raised to 165–170°, two isomeric dicarboxylic acids are obtained, *rhodophylline* and *erythrophylline*, which differ from the two acids described above in color and chemical properties. Just what causes this isomerism is not known. Willstätter suggests that they differ by the presence of two hydrogen atoms. By increasing the temperature another 20 degrees (195° to 200°), the second carboxyl group is split off, probably the  $\beta$  carboxyl. Then *pyrrophylline* and *phyllophylline* result. They can differ only in the position of the carboxyl group, *pyrrophylline* probably containing the  $\alpha$  carboxyl, while *phyllophylline* contains the  $\gamma$  carboxyl group. They have the formula,



As is seen from the table on page 241, these two products are common to both components of chlorophyll, *a* and *b*. For this rea-

<sup>29</sup> Willstätter, Fischer and Forsén: *Ann. d. Chem.*, 400, 147 (1913).



son they may be prepared from a mixture of these two components. Chlorophylline ( $a + b$ ) is suitable for the preparation of pyrrophylline, while phyllophylline may be obtained from isochlorophylline ( $a + b$ ). Twenty gm. of crude potassium chlorophylline salt, dissolved in 400 c.c. of 35 percent methyl alcoholic potash sol., are heated in a silver beaker slowly to  $130^{\circ}$ , the temperature held two hours between  $130^{\circ}$ – $135^{\circ}$ , then raised during the course of an hour to  $170^{\circ}$ , held for two hours between  $170^{\circ}$ – $180^{\circ}$ , then raised to  $190^{\circ}$  during an hour and a half, and finally held about  $200^{\circ}$  for one hour. The cold mass is diluted with two vol. of water, which precipitates the potassium salt as violet crystalline flakes. The product is filtered off, rubbed into a paste with alcohol and ether, and poured into 5 liters of ether. Shaken with 20 gm. of monosodium phosphate crystals, the greater part of the pyrrophylline goes into the ether. This solution is washed with dilute sodium phosphate sol. and water, then extracted with 0.03 percent ammonia which removes all rhodophylline. The solution is then conc. to 50 c.c., poured into 1 liter of petroleum ether and allowed to stand several days at  $0^{\circ}$ , when the phylline precipitates as a violet red powder; yield, 8.5 gm.

Phyllophylline is obtained in nearly the same manner, in a yield of 70 percent, as the calcium salt. The free substance is quite unstable and easily loses its magnesium. The compound is also prepared from pheophytin ( $a + b$ ) by the action of methyl alcoholic potash sol. containing magnesium oxide, by heating for eight hours up to  $205^{\circ}$  and then three hours at this temperature. The yield from 20 gm. was 6.7 gm. of the calcium salt.

The corresponding porphyrines may be obtained by shaking the phyllines with acetic or hydrochloric acid. They may also be prepared from the magnesium-free derivatives of chlorophyll by heating with methyl alcoholic potash sol. Phytochlorine *c* gives phylloporphyrine when heated several hours at  $140^{\circ}$ – $150^{\circ}$ . The less basic chlorines give pyrroporphyrine when heated to  $220$ – $230^{\circ}$ . The reaction in the *b* series is best carried out in the presence of pyridine.

The principal properties and a comparison of the various derivatives in this group are shown in the table on page 251.

The use of methyl alcoholic potash sol. readily gives a monocarboxylic acid. If an attempt is made to heat the reaction-mixture



higher, to 250° for example, brown amorphous products result besides hemopyrrole and carboxyl-free derivatives can not be obtained. Heating with quinoline or acridine was without effect. The last

*Data pertaining to phyllines and porphyrines*

*A. Phyllines*

	Glauco- phylline	Cyano- phylline	Rhodo- phylline	Erythro- phylline	Rubi- phylline	Pyno- phylline	Phyllo- phylline
Color (in ether)	Blue	Blue	Bluish red	Red	Violet red	Bluish red	Bluish red
Chloroform	Insoluble					Soluble	
Ammonia (n/10)	Completely extracted from ether					Insoluble	
Solubility of the ammonium salt in ether	Insoluble			Soluble	Insoluble	Insoluble	Soluble
Behavior towards disodium phosphate	Extracted from ether by 0.3 per cent.			Completely extracted by 1 per cent.	Not extracted by 0.5, but by 1 per cent.	Insoluble	

*B. Porphyrines*

	Glauco- por- phyrine	Cyano- por- phyrine	Rhodo- por- phyrine	Erythro- por- phyrine	Rubi- por- phyrine	Pyrro- por- phyrine	Phyllo- pro- phyrine
Color (in ether)	Bluish red		Brownish red	Light red	Red	Brownish red	
Color (in HCl—20 per cent.)	Red violet	Blue green	Red violet	Pure red	Reddish blue	Bluish red	Brownish red
Color (in HCl—4 per cent.)	Blue violet	Blue	Bluish violet	Violet red	Bluish red	Blue red	Violet red
Solubility of the HCl salt in dilute HCl	Easily soluble		Slightly soluble	Insoluble	Slightly soluble	Slightly soluble	Easily soluble
Acid number	3.5	4	3	—	4.5	1.5	0.75

carboxyl group may be removed, however, by heating for a short time with soda-lime in a test tube, small amounts of material being used and the temperature conditions being carefully regulated. The phyllines decompose easier and give cleaner reaction-products than the porphyrines, so that the best method for preparing carboxyl-free porphyrine is through the phylline.

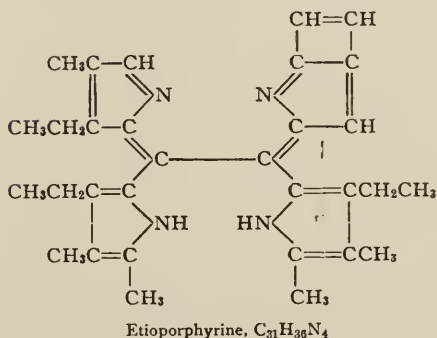
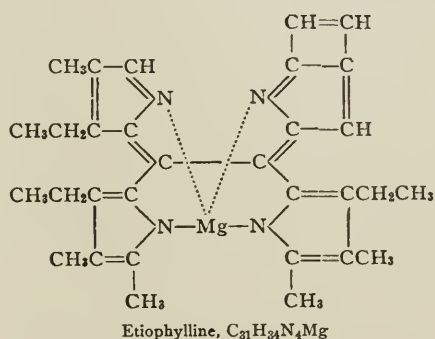
*Etiophylline*<sup>30</sup> is obtained as follows: Potassium rhodophylline is rubbed with four or five parts of pure (iron-free) soda-lime and heated in lots of 0.05 to 0.1 gm. of the salt over a free flame until the color changes from a light gray to a brown, and the odor of hemopyrrole becomes evident. At this point the heating is discontinued and the tube quickly cooled. The contents are moistened with a little water and shaken with ether. The ether sol. is shaken with methyl alcoholic potash sol., the potash layer diluted with water, the ether shaken with 5 percent hydrochloric acid, then with ammonia, conc. to 2 c.c., and the product recrystallized from 1 c.c. of ether. The yield from 10 gm. of the salt is 0.4 gm. of pure substance. This yields nearly 8 percent of pure magnesium oxide, when ashed. It has the composition indicated by the formula,  $C_{31}H_{34}N_4Mg$ ; forms thick rose or blue-violet tables or prisms from ether, deep red rhombic tables from petroleum ether. The ether sol. is stable towards 4 or 7 percent hydrochloric acid and is first decomposed by 15 percent hydrochloric acid. In petroleum ether it is decomposed by 0.5 percent acid, completely by 3 percent. The alcoholic sol. is bluish red with strong fluorescence; diluted, it is violet.

*Etioporphyrine* is best prepared by shaking the ether sol. of the phylline with 20 percent hydrochloric acid, neutralizing the product with ammonia and extracting with ether, from which it may be shaken out with 4 percent hydrochloric acid. It may also be prepared by heating phyllo-, pyrro- or rhodoporphyrine with soda-lime, until vapors are given off. Treated with methyl magnesium iodide, it gives the phylline. It has the composition indicated by the formula,  $C_{31}H_{36}N_4$ ; has a violet color, giving a brownish red alcoholic sol. and a bluish red sol. in formic acid. It forms characteristic complex compounds with the salts of the heavy metals. The acetic acid sol. warmed with zinc acetate gives a pure red sol., while cop-

<sup>30</sup> Willstätter and Fischer: *Ann. d. Chem.*, 400, 182 (1913).

per acetate gives a violet red. It also gives salts with picric acid, platinic chloride and hydrochloric acid. The styphnate forms aggregates of red prisms, which may be used for identification purposes. The hydrochloride forms long olive brown needles.

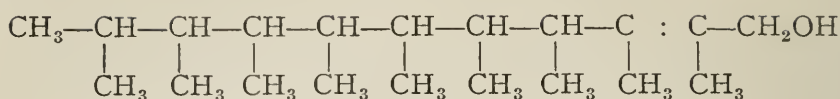
The two compounds have also been obtained from hemoporphyrine, one of the decomposition products of the coloring matter of the blood, hemin. From a consideration of the reactions of hemin and its decomposition products, Willstätter suggests the following as working formulas for etiophylline and etioporphyrine.<sup>31</sup>



**Phytol.**<sup>32</sup> Phytol is the characteristic alcoholic component of chlorophyll, comprising about one third of the molecule. It is split off by the enzyme, chlorophyllase, or by hydrolysis with alkali. It is an unsaturated, primary alcohol of the fatty series, having the composition,  $C_{20}H_{40}O$ , and from its reactions probably has the constitution:

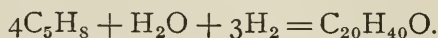
<sup>31</sup> Willstätter and Fischer: *Zeit. f. physiol. Chem.*, **87**, 423 (1913).

<sup>32</sup> Willstätter, Meyer and Hünig: *Ann. d. Chem.*, **378**, 73 (1910).



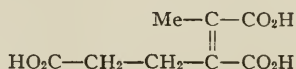
The unsaturated nature of the alcohol is shown by the fact that it adds one molecule of bromine and that it takes up one molecule of hydrogen to form dihydrophytol,  $\text{C}_{20}\text{H}_{42}\text{O}$ . It is easily oxidized by chromic acid or by ozone, forming a ketone,  $\text{C}_{17}\text{H}_{34}\text{O}$ . When this ketone is treated with oxidizing agents, a series of ketones is obtained by successive removal of pairs of carbon atoms, together with saturated acids which contain one carbon less than the ketonic products; this indicates the ketomethyl,  $-\text{COCH}_3$ , arrangement. These methyl ketones from phytol are interesting not only on account of their bearing upon the structure of that substance, but also because of certain anomalies in their physical properties. An explanation of the latter has been sought in the assumption that the samples obtained consisted of the enolic isomerides.

As an explanation of the natural synthesis of this substance, it has been pointed out that the peculiar structure of the alcohol suggests that it is formed by polymerization of a hydrocarbon such as isoprene, four molecules being condensed by the intervention of water and hydrogen:



In spite of the slender basis on which this hypothesis lies, it is particularly attractive on account of the genetic connection which it reveals between phytol and the terpenes, rubbers and other groups of compounds.

**Oxidation of chlorophyll derivatives.** The only early reference to the oxidation of chlorophyll derivatives is that of Marchlewski,<sup>33</sup> who oxidized phylloporphyrine with chromic acid and obtained hematinic acid:

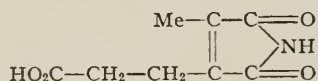


Under the same conditions Küster<sup>34</sup> had previously obtained the

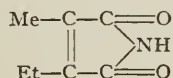
<sup>33</sup> Marchlewski: *Bull. de l'Acad. des Sciences de Cracovie*, 1902, 1.

<sup>34</sup> Küster: *Zeitschr. f. physiol. Chem.*, 28, 1 (1899); 29, 185 (1900); 44, 391 (1905); 54, 501 (1908); 61, 164 (1909).

same acid from hemin, but in the form of the imide:



Willstätter<sup>35</sup> has shown that, by the oxidation of chlorophyll derivatives (phyllo-, pyrro-, and rhodo-porphyrines, and phytochlorine) with either lead peroxide and sulfuric acid, chromic acid, or Caro's acid, there results a mixture, which, apart from minor decomposition products, such as carbon dioxide and acetic acid, consists of two principal products: hematinic acid imide and methyl-ethyl maleinic imide.



The latter compound had been obtained by Küster<sup>36</sup> by splitting off carbon dioxide from the hematinic acid imide, and had also been prepared synthetically by him. It was not obtained by the oxidation of hemin.

The oxidation is best carried out by dissolving the chlorophyll derivative in about 50 percent sulfuric acid, cooling to 0°, adding a solution of chromic acid in water with stirring and holding the temperature at 5-7°. The next day the sol. is filtered, extracted with ether, the mixture dissolved in water after the removal of the ether, neutralized with sodium carbonate and extracted with ether, when the two substances are obtained crystalline. Five gm. of phylloporphyrine gave about 3.3 gm. of the mixture, of which 1.67 gm. was methyl-ethyl maleinic acid and 1.3 gm. hematinic acid imide. This is approximately one molecule of each. Willstätter supposes, however, that since the yield of methyl-ethyl maleinic imide is always a little larger than that required for one molecule, and since there is always a certain amount of loss connected with the purification, two pyrrole nuclei are concerned in the formation of this compound.

Since methyl-ethyl maleinic imide is not formed in the oxidation of hemin, at least two of the four pyrrole nuclei in chlorophyll are different from those of hemin.

<sup>35</sup> Willstätter and Asahina: *Ann. d. Chem.*, 373, 227 (1910).

<sup>36</sup> Küster: *Ibid.*, 315, 174 (1900).



**Reduction of chlorophyll derivatives.** A further relationship between the coloring matter of the blood and that of the green plants is found in their behavior towards reducing agents. This work was first undertaken by Nencki,<sup>37</sup> who isolated hemopyrrole from both hemin and phylloporphyrine. Nencki's death occurred shortly after the publication of this finding and the work was discontinued as a consequence. Work on the pyrroles obtained from hemin was carried on later by Piloty<sup>38</sup> and Küster.<sup>39</sup> They showed that the reduction mixture probably consists of pyrroles and pyrrolines (reduced pyrroles), but thought pyrrole to be homogeneous. The work of Willstätter and Asahina<sup>40</sup> showed that the products of the reduction of the two classes of dyes were similar, but that a complex mixture of pyrrole homologues was formed and not a single pyrrole, as has just been mentioned.

The reduction was carried out essentially according to Nencki and Zaleski. Twenty-five gm. of hemin were heated with a mixture of 450 c.c. of acetic acid and 500 gm. of hydriodic acid (d. 1.96), 1.5 hours on a water-bath. After solution was complete, 20 gm. of phosphonium iodide were added in small portions, in the course of half an hour, the light yellow sol. then diluted with 1.5 vol. of water and anhydrous sodium carbonate added until the reaction mixture was alkaline. The bases were distilled with steam, extracted with ether, and the ether sol. washed with 30 percent monosodium phosphate sol., which quantitatively removed the hydrogenated pyrrole bases (secondary products of the reaction).

More difficulty was found in separating the purified hemopyrrole mixture. Fractional distillation in vacuum was of little use. Fractional crystallization of the picrates did not yield good results. Finally a satisfactory method was found in the fractional salt formation with picric acid and, by the repeated use of this method, three components were isolated, two of which, at least, were pure.

The one which may not be pure is *hemopyrrole*, the picrate of

<sup>37</sup> Nencki and Zaleski: *Ber. d. deutsch. chem. Gesellsch.*, 34, 997 (1901); Nencki and Marchlewski: *Ibid.*, 34, 1687 (1901).

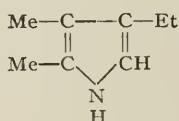
<sup>38</sup> Piloty: *Ann. d. Chem.*, 366, 237 (1909); 377, 314 (1910); Piloty and Quitmann: *Ber. d. deutsch. chem. Gesellsch.*, 42, 4693 (1909).

<sup>39</sup> Küster: *Ann. d. Chem.*, 346, 1 (1906); *Zeitschr. f. physiol. Chem.*, 55, 526 (1908).

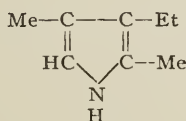
<sup>40</sup> Willstätter and Asahina: *Ann. d. Chem.*, 385, 188 (1911).

which melts at  $108-9^{\circ}$ . With nitrous acid it gives methyl-ethyl maleinic-imide oxime, melting at  $201^{\circ}$ . This has been considered by Piloty and Stock<sup>41</sup> to be a mixture. This compound was later named *kryptopyrrole*.<sup>42</sup> It has been synthesized by Knorr and Hess.<sup>43</sup>

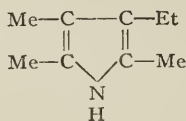
A second base, *isohemopyrrole*, was isolated in a pure state, which melts at  $16-7^{\circ}$ ,  $b_{11-12}$ ,  $88^{\circ}$ ; the picrate melts at  $119^{\circ}$ ; with nitrous acid, isohemopyrrole gives the second oxime of methyl-ethyl maleinic imide, melting at  $219^{\circ}$ . The styphnate forms yellow prisms, melting at  $136^{\circ}$ .



Isohemopyrrole



Kryptopyrrole



Phyllopyrrole

The third base, *phyllopyrrole*, is the most interesting. This has been prepared synthetically by Fischer<sup>44</sup> and its constitution established. It melts at  $66-67^{\circ}$ . The picrate, which is the most easily soluble of the three, melts at  $95^{\circ}$ . It does not show the dimethyl amino benzaldehyde reaction<sup>45</sup> nor the pine-stick reaction. It is not precipitated by aqueous mercuric chloride. That it is a pyrrole is indicated by the fact that it may be reduced to a tetrahydro-base. It forms a potassium salt with the evolution of hydrogen.

Of the chlorophyll derivatives investigated, phylloporphyrin gives the largest yield of volatile reduction-product because it contains only one carboxyl. Concerning the role of the four nitrogen-containing nuclei of phylloporphyrine in reduction and oxidation, the following may be stated: Two nuclei give, upon reduction, tri-substituted pyrroles. They are the same as those which give methyl-

<sup>41</sup> Piloty and Stock: *Ann. d. Chem.*, **392**, 215 (1912); *Ber. d. deutsch. chem. Gesellsch.*, **46**, 1008 (1913).

<sup>42</sup> Fischer and Bartholomäus: *Ber. d. deutsch. chem. Gesellsch.*, **45**, 1979 (1912).

<sup>43</sup> Knorr and Hess: *Ber. d. deutsch. chem. Gesellsch.*, **44**, 2578 (1911).

<sup>44</sup> Fischer and Bartholomäus: *Ber. d. deutsch. chem. Gesellsch.*, **45**, 466 (1912); *Zeitschr. f. physiol. Chem.*, **77**, 185 (1912); cf. Colacicchi: *Atti R. Accad. dei Lincei*, **21** (I), 489, 653 (1912).

<sup>45</sup> Ehrlich: *Die med. Woche*, 1901, 151; Neubauer: *Verhandl. d. Gesellsch. d. Naturf. u. Ärzte*, **2**, 68 (1903).

ethyl maleinic imide upon oxidation. One nucleus gives upon reduction phyllopyrrole; this is probably the same one that is lost upon oxidation. The fourth behaves in reduction as it does in the oxidation of its carboxyl—it does not form a volatile pyrrole derivative. Upon oxidation it gives the imide of hematinic acid.

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# TABLES OF THE RELATIVE DEPRESSION OF THE FREEZING POINT, $1.860/\Delta$ , TO FACILITATE THE CALCULATION OF MOLECULAR WEIGHTS

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The molecular weight of a substance is given by  $C \times K/\Delta$ , where  $C = \frac{\text{weight of solute}}{\text{weight of solvent}}$ ,  $K = 1000 \times$  the molecular lowering for a given solvent, and  $\Delta =$  the depression of the freezing point in degrees centigrade. While the arithmetic of these calculations is not onerous it is clear that tables for  $K/\Delta$  will be of considerable service. We have found them indispensable in dealing with large series of determinations of the mean molecular weight of the solutes in vegetable saps.

The selection of the proper value from those which have been used for the molecular lowering, *i. e.*, the depression of the freezing point produced by dissolving one mole of solute in 1000 grams of water, is the only point requiring consideration. We follow the more recent texts on physical chemistry in taking the value as roundly  $1.86^\circ$ .<sup>1</sup>

<sup>1</sup> D. Berthelot's (*Z. f. Elektrochemie*, 10, 621-629; 1904) analysis of the experimental determinations results in 22.412 l. as the volume of a gram molecule of gas under standard conditions,  $273.09^\circ$  as the melting point of ice on the absolute scale, and  $22.412/273.09 = 0.082086 = R$ , the gas constant. Taken in connection with the equation

$$P = 12.06\Delta - 0.021\Delta^2$$

for the calculation of osmotic pressure from the depression of the freezing point as used in our table [Harris, J. Arthur, and Gortner, Ross Aiken, *Notes on the Calculation of the Osmotic Pressure of Expressed Vegetable Saps from the Depression of the Freezing Point with a Table of Values for P from  $\Delta = 0.001^\circ$  to  $\Delta = 2.999^\circ$*  (in press)], and on the assumption that Van't Hoff's law holds rigidly this gives (compare Lewis, G. N., *J. Amer. Chem. Soc.*, 30, 670; 1908)  $1.858^\circ$  as the molecular lowering. In view of the widely varying practice of physical chemists we have, however, used the round number generally employed,  $1.86^\circ$  instead of the theoretical  $1.858^\circ$ . Those who may desire for any reason to use another value for the molecular lowering may do so by making use of a factor.

TABLE 1\*

$$\Delta = 0.001^\circ - \Delta = 0.399^\circ$$

$\Delta$	0	1	2	3	4	5	6	7	8	9
0.00	—	—	930,000	620,000	465,000	372,000	310,000	265,714	232,500	206,667
0.01	186,000	169,091	155,000	143,077	132,857	124,000	116,250	109,412	103,333	97,895
0.02	93,000	88,571	84,545	80,870	77,500	74,400	71,538	68,889	66,429	64,138
0.03	62,000	60,000	58,125	56,364	54,706	53,143	51,667	50,270	48,947	47,692
0.04	46,500	45,366	44,286	43,256	42,273	41,333	40,435	39,574	38,750	37,959
0.05	37,200	36,471	35,769	35,094	34,444	33,818	33,214	32,632	32,069	31,525
0.06	31,000	30,492	30,000	29,524	29,063	28,615	28,182	27,761	27,353	26,957
0.07	26,571	26,197	25,833	25,479	25,135	24,800	24,474	24,156	23,846	23,544
0.08	23,250	22,963	22,683	22,410	22,143	21,882	21,628	21,379	21,136	20,899
0.09	20,667	20,440	20,217	20,000	19,787	19,579	19,375	19,175	18,980	18,788
0.10	18,600	18,416	18,235	18,058	17,885	17,714	17,547	17,383	17,222	17,064
0.11	16,909	16,757	16,607	16,460	16,316	16,174	16,034	15,897	15,763	15,630
0.12	15,500	15,372	15,246	15,122	15,000	14,880	14,762	14,646	14,531	14,419
0.13	14,308	14,198	14,091	13,985	13,881	13,778	13,676	13,577	13,478	13,381
0.14	13,286	13,191	13,099	13,007	12,917	12,828	12,740	12,653	12,568	12,483
0.15	12,400	12,318	12,237	12,157	12,078	12,000	11,923	11,847	11,772	11,698
0.16	11,625	11,553	11,481	11,411	11,341	11,273	11,205	11,138	11,071	11,006
0.17	10,941	10,877	10,814	10,751	10,690	10,629	10,568	10,508	10,449	10,391
0.18	10,333	10,276	10,220	10,164	10,109	10,054	10,000	9,946.5	9,893.6	9,841.2
0.19	9,789.4	9,738.2	9,687.5	9,637.3	9,587.6	9,538.4	9,489.7	9,441.6	9,393.9	9,346.7
0.20	9,300.0	9,253.7	9,207.9	9,162.5	9,117.6	9,073.1	9,029.1	8,985.5	8,942.3	8,899.5
0.21	8,857.1	8,815.1	8,773.5	8,732.3	8,691.5	8,651.1	8,611.1	8,571.4	8,532.1	8,493.1
0.22	8,454.5	8,416.2	8,378.3	8,340.8	8,303.5	8,266.6	8,230.0	8,193.8	8,157.8	8,122.2
0.23	8,086.9	8,051.9	8,017.2	7,982.8	7,948.7	7,914.8	7,881.3	7,848.1	7,815.1	7,782.4
0.24	7,750.0	7,717.8	7,685.9	7,654.3	7,622.9	7,591.8	7,560.9	7,530.3	7,500.0	7,469.8
0.25	7,440.0	7,410.3	7,380.9	7,351.7	7,322.8	7,294.1	7,265.6	7,237.3	7,209.3	7,181.4
0.26	7,153.8	7,126.4	7,099.2	7,072.2	7,045.4	7,018.8	6,992.4	6,966.2	6,940.2	6,914.5
0.27	6,888.8	6,863.4	6,838.2	6,813.1	6,788.3	6,763.6	6,739.1	6,714.8	6,690.6	6,666.6
0.28	6,642.8	6,619.2	6,595.7	6,572.4	6,549.2	6,526.3	6,503.4	6,480.8	6,458.3	6,435.9
0.29	6,413.7	6,391.7	6,369.8	6,348.1	6,326.5	6,305.0	6,283.7	6,262.6	6,241.6	6,220.7
0.30	6,200.0	6,179.4	6,158.9	6,138.6	6,118.4	6,098.3	6,078.4	6,058.6	6,038.9	6,019.4
0.31	6,000.0	5,980.7	5,961.5	5,942.4	5,923.5	5,904.7	5,886.0	5,867.5	5,849.0	5,830.7
0.32	5,812.5	5,794.3	5,776.3	5,758.5	5,740.7	5,723.0	5,705.5	5,688.0	5,670.7	5,653.4
0.33	5,636.3	5,619.3	5,602.4	5,585.5	5,568.8	5,552.2	5,535.7	5,519.2	5,502.9	5,486.7
0.34	5,470.5	5,454.5	5,438.5	5,422.7	5,406.9	5,391.3	5,375.7	5,360.2	5,344.8	5,329.5
0.35	5,314.2	5,299.1	5,284.0	5,269.1	5,254.2	5,239.4	5,224.7	5,210.0	5,195.5	5,181.0
0.36	5,166.6	5,152.3	5,138.1	5,123.9	5,109.8	5,095.8	5,081.9	5,068.1	5,054.3	5,040.6
0.37	5,027.0	5,013.4	5,000.0	4,986.5	4,973.2	4,960.0	4,946.8	4,933.6	4,920.6	4,907.6
0.38	4,894.7	4,881.8	4,869.1	4,856.3	4,843.7	4,831.1	4,818.6	4,806.2	4,793.8	4,781.4
0.39	4,769.2	4,757.0	4,744.8	4,732.8	4,720.8	4,708.8	4,696.9	4,685.1	4,673.3	4,661.6

\* In Table 1 are given the relative depressions,  $1860/\Delta$ , for  $\Delta = 0.001^\circ$  to  $\Delta = 1.199^\circ$ , in intervals of  $1/1000^\circ$ . Beyond this point it seems unnecessary to give values for intervals of less than  $1/100^\circ$ , since (a) the range of values already given will be most frequently met with in practice, and (b) for values beyond  $1.199^\circ$  linear interpolation may be used. Table 2 gives values for  $\Delta = 1.20^\circ$  to  $\Delta = 3.49^\circ$ .



TABLE I (continued)\*

$$\Delta = 0.400^\circ - \Delta = 0.799^\circ$$

$\Delta$	0	1	2	3	4	5	6	7	8	9
0.40	4,650.0	4,638.4	4,626.8	4,615.3	4,603.9	4,592.5	4,581.2	4,570.0	4,558.8	4,547.6
0.41	4,536.5	4,525.5	4,514.5	4,503.6	4,492.7	4,481.9	4,471.1	4,460.4	4,449.7	4,439.1
0.42	4,428.5	4,418.0	4,407.5	4,397.1	4,386.7	4,376.4	4,366.1	4,355.9	4,345.7	4,335.6
0.43	4,325.5	4,315.5	4,305.5	4,295.6	4,285.7	4,275.8	4,266.0	4,256.2	4,246.5	4,236.9
0.44	4,227.2	4,217.6	4,208.1	4,198.6	4,189.1	4,179.7	4,170.4	4,161.0	4,151.7	4,142.5
0.45	4,133.3	4,124.1	4,115.0	4,105.9	4,096.9	4,087.9	4,078.9	4,070.0	4,061.1	4,052.2
0.46	4,043.4	4,034.7	4,025.9	4,017.2	4,008.6	4,000.0	3,991.4	3,982.8	3,974.3	3,965.8
0.47	3,957.4	3,949.0	3,940.6	3,932.3	3,924.0	3,915.7	3,907.5	3,899.3	3,891.2	3,883.0
0.48	3,875.0	3,866.9	3,858.9	3,850.9	3,842.9	3,835.0	3,827.1	3,819.3	3,811.4	3,803.6
0.49	3,795.9	3,788.1	3,780.4	3,772.8	3,765.1	3,757.5	3,750.0	3,742.4	3,734.9	3,727.4
0.50	3,720.0	3,712.5	3,705.1	3,697.8	3,690.4	3,683.1	3,675.8	3,668.6	3,661.4	3,654.2
0.51	3,647.0	3,639.9	3,632.8	3,625.7	3,618.6	3,611.6	3,604.6	3,597.6	3,590.7	3,583.8
0.52	3,576.9	3,570.0	3,563.2	3,556.4	3,549.6	3,542.8	3,536.1	3,529.4	3,522.7	3,516.0
0.53	3,509.4	3,502.8	3,496.2	3,489.6	3,483.1	3,476.6	3,470.1	3,463.6	3,457.2	3,450.8
0.54	3,444.4	3,438.0	3,431.7	3,425.4	3,419.1	3,412.8	3,406.5	3,400.3	3,394.1	3,387.9
0.55	3,381.8	3,375.6	3,369.5	3,363.4	3,357.4	3,351.3	3,345.3	3,339.3	3,333.3	3,327.3
0.56	3,321.4	3,315.5	3,309.6	3,303.7	3,297.8	3,292.0	3,286.2	3,280.4	3,274.6	3,268.8
0.57	3,263.1	3,257.4	3,251.7	3,246.0	3,240.4	3,234.7	3,229.1	3,223.5	3,217.9	3,212.4
0.58	3,206.8	3,201.3	3,195.8	3,190.3	3,184.9	3,179.4	3,174.0	3,168.6	3,163.2	3,157.8
0.59	3,152.5	3,147.2	3,141.8	3,136.5	3,131.3	3,126.0	3,120.8	3,115.5	3,110.3	3,105.1
0.60	3,100.0	3,094.8	3,089.7	3,084.5	3,079.4	3,074.3	3,069.3	3,064.2	3,059.2	3,054.1
0.61	3,049.1	3,044.1	3,039.2	3,034.2	3,029.3	3,024.3	3,019.4	3,014.5	3,009.7	3,004.8
0.62	3,000.0	2,995.1	2,990.3	2,985.5	2,980.7	2,976.0	2,971.2	2,966.5	2,961.7	2,957.0
0.63	2,952.3	2,947.7	2,943.0	2,938.3	2,933.7	2,929.1	2,924.5	2,919.9	2,915.3	2,910.7
0.64	2,906.2	2,901.7	2,897.1	2,892.6	2,888.1	2,883.7	2,879.2	2,874.8	2,870.3	2,865.9
0.65	2,861.5	2,857.1	2,852.7	2,848.3	2,844.0	2,839.6	2,835.3	2,831.0	2,826.7	2,822.4
0.66	2,818.1	2,813.9	2,809.6	2,805.4	2,801.2	2,796.9	2,792.7	2,788.6	2,784.4	2,780.2
0.67	2,776.1	2,771.9	2,767.8	2,763.7	2,759.6	2,755.5	2,751.4	2,747.4	2,743.3	2,739.3
0.68	2,735.2	2,731.2	2,727.2	2,723.2	2,719.2	2,715.3	2,711.3	2,707.4	2,703.4	2,699.5
0.69	2,695.6	2,691.7	2,687.8	2,683.9	2,680.1	2,676.2	2,672.4	2,668.5	2,664.7	2,660.9
0.70	2,657.1	2,653.3	2,649.5	2,645.8	2,642.0	2,638.2	2,634.5	2,630.8	2,627.1	2,623.4
0.71	2,619.7	2,616.0	2,612.3	2,608.6	2,605.0	2,601.3	2,597.7	2,594.1	2,590.5	2,586.9
0.72	2,583.3	2,579.7	2,576.1	2,572.6	2,569.0	2,565.5	2,561.9	2,558.4	2,554.9	2,551.4
0.73	2,547.9	2,544.4	2,540.9	2,537.5	2,534.0	2,530.6	2,527.1	2,523.7	2,520.3	2,516.9
0.74	2,513.5	2,510.1	2,506.7	2,503.3	2,500.0	2,496.6	2,493.2	2,489.9	2,486.6	2,483.3
0.75	2,480.0	2,476.6	2,473.4	2,470.1	2,466.8	2,463.5	2,460.3	2,457.0	2,453.8	2,450.5
0.76	2,447.3	2,444.1	2,440.9	2,437.7	2,434.5	2,431.3	2,428.1	2,425.0	2,421.8	2,418.7
0.77	2,415.5	2,412.4	2,409.3	2,406.2	2,403.1	2,400.0	2,396.9	2,393.8	2,390.7	2,387.6
0.78	2,384.6	2,381.5	2,378.5	2,375.4	2,372.4	2,369.4	2,366.4	2,363.4	2,360.4	2,357.4
0.79	2,354.4	2,351.4	2,348.4	2,345.5	2,342.5	2,339.6	2,336.6	2,333.7	2,330.8	2,327.9

\* See the footnote on the opposite page.

TABLE I (continued)\*

$$\Delta = 0.800^\circ - \Delta = 1.199^\circ$$

$\Delta$	0	1	2	3	4	5	6	7	8	9
0.80	2,325.0	2,322.0	2,319.2	2,316.3	2,313.4	2,310.5	2,307.6	2,304.8	2,301.9	2,299.1
0.81	2,296.2	2,293.4	2,290.6	2,287.8	2,285.0	2,282.2	2,279.4	2,276.6	2,273.8	2,271.0
0.82	2,268.2	2,265.5	2,262.7	2,260.0	2,257.2	2,254.5	2,251.8	2,249.0	2,246.3	2,243.6
0.83	2,240.9	2,238.2	2,235.5	2,232.8	2,230.2	2,227.5	2,224.8	2,222.2	2,219.5	2,216.9
0.84	2,214.2	2,211.6	2,209.0	2,206.4	2,203.7	2,201.1	2,198.5	2,195.9	2,193.3	2,190.8
0.85	2,188.2	2,185.6	2,183.0	2,180.5	2,177.9	2,175.4	2,172.8	2,170.3	2,167.8	2,165.3
0.86	2,162.7	2,160.2	2,157.7	2,155.2	2,152.7	2,150.2	2,147.8	2,145.3	2,142.8	2,140.3
0.87	2,137.9	2,135.4	2,133.0	2,130.5	2,128.1	2,125.7	2,123.2	2,120.8	2,118.4	2,116.0
0.88	2,113.6	2,111.2	2,108.8	2,106.4	2,104.0	2,101.6	2,099.3	2,096.9	2,094.5	2,092.2
0.89	2,089.8	2,087.5	2,085.2	2,082.8	2,080.5	2,078.2	2,075.8	2,073.5	2,071.2	2,068.9
0.90	2,066.6	2,064.3	2,062.0	2,059.8	2,057.5	2,055.2	2,052.9	2,050.7	2,048.4	2,046.2
0.91	2,043.9	2,041.7	2,039.4	2,037.2	2,035.0	2,032.7	2,030.5	2,028.3	2,026.1	2,023.9
0.92	2,021.7	2,019.5	2,017.3	2,015.1	2,012.9	2,010.8	2,008.6	2,006.4	2,004.3	2,002.1
0.93	2,000.0	1,997.8	1,995.7	1,993.5	1,991.4	1,989.3	1,987.1	1,985.0	1,982.9	1,980.8
0.94	1,978.7	1,976.6	1,974.5	1,972.4	1,970.3	1,968.2	1,966.1	1,964.0	1,962.0	1,959.9
0.95	1,957.8	1,955.8	1,953.7	1,951.7	1,949.6	1,947.6	1,945.6	1,943.5	1,941.5	1,939.5
0.96	1,937.5	1,935.4	1,933.4	1,931.4	1,929.4	1,927.4	1,925.4	1,923.4	1,921.4	1,919.5
0.97	1,917.5	1,915.5	1,913.5	1,911.6	1,909.6	1,907.6	1,905.7	1,903.7	1,901.8	1,899.8
0.98	1,897.9	1,896.0	1,894.0	1,892.1	1,890.2	1,888.3	1,886.4	1,884.4	1,882.5	1,880.6
0.99	1,878.7	1,876.8	1,875.0	1,873.1	1,871.2	1,869.3	1,867.4	1,865.5	1,863.7	1,861.8
1.00	1,860.0	1,858.1	1,856.2	1,854.4	1,852.5	1,850.7	1,848.9	1,847.0	1,845.2	1,843.4
1.01	1,841.5	1,839.7	1,837.9	1,836.1	1,834.3	1,832.5	1,830.7	1,828.9	1,827.1	1,825.3
1.02	1,823.5	1,821.7	1,819.9	1,818.1	1,816.4	1,814.6	1,812.8	1,811.1	1,809.3	1,807.5
1.03	1,805.8	1,804.0	1,802.3	1,800.5	1,798.8	1,797.1	1,795.3	1,793.6	1,791.9	1,790.1
1.04	1,788.4	1,786.7	1,785.0	1,783.3	1,781.6	1,779.9	1,778.2	1,776.5	1,774.8	1,773.1
1.05	1,771.4	1,769.7	1,768.0	1,766.3	1,764.7	1,763.0	1,761.3	1,759.6	1,758.0	1,756.3
1.06	1,754.7	1,753.0	1,751.4	1,749.7	1,748.1	1,746.4	1,744.8	1,743.2	1,741.5	1,739.9
1.07	1,738.3	1,736.6	1,735.0	1,733.4	1,731.8	1,730.2	1,728.6	1,727.0	1,725.4	1,723.8
1.08	1,722.2	1,720.6	1,719.0	1,717.4	1,715.8	1,714.2	1,712.7	1,711.1	1,709.5	1,707.9
1.09	1,706.4	1,704.8	1,703.2	1,701.7	1,700.1	1,698.6	1,697.0	1,695.5	1,693.9	1,692.4
1.10	1,690.9	1,689.3	1,687.8	1,686.3	1,684.7	1,683.2	1,681.7	1,680.2	1,678.7	1,677.1
1.11	1,675.6	1,674.1	1,672.6	1,671.1	1,669.6	1,668.1	1,666.6	1,665.1	1,663.6	1,662.1
1.12	1,660.7	1,659.2	1,657.7	1,656.2	1,654.8	1,653.3	1,651.8	1,650.3	1,648.9	1,647.4
1.13	1,646.0	1,644.5	1,643.1	1,641.6	1,640.2	1,638.7	1,637.3	1,635.8	1,634.4	1,633.0
1.14	1,631.5	1,630.1	1,628.7	1,627.2	1,625.8	1,624.4	1,623.0	1,621.6	1,620.2	1,618.7
1.15	1,617.3	1,615.9	1,614.5	1,613.1	1,611.7	1,610.3	1,608.9	1,607.6	1,606.2	1,604.8
1.16	1,603.4	1,602.0	1,600.6	1,599.3	1,597.9	1,596.5	1,595.1	1,593.8	1,592.4	1,591.1
1.17	1,589.7	1,588.3	1,587.0	1,585.6	1,584.3	1,582.9	1,581.6	1,580.2	1,578.9	1,577.6
1.18	1,576.2	1,574.9	1,573.6	1,572.2	1,570.9	1,569.6	1,568.2	1,566.9	1,565.6	1,564.3
1.19	1,563.0	1,561.7	1,560.4	1,559.0	1,557.7	1,556.4	1,555.1	1,553.8	1,552.5	1,551.2

\* See the footnote on page 260.

TABLE 2  
 $\Delta = 1.20^\circ - \Delta = 3.190^\circ$

$\Delta$	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.8	3.0
0	1,550.0 12.9	1,328.5 9.4	1,162.5 7.3	1,033.3 5.7	930.00 4.63	845.45 3.83	775.00 3.22	715.38 2.74	664.28 2.36	620.00 2.06
1	1,537.1 12.6	1,319.1 9.3	1,155.2 7.1	1,027.6 5.7	925.37 4.58	841.62 3.79	771.78 3.19	712.64 2.72	661.92 2.35	617.94 2.05
2	1,524.5 12.4	1,309.8 9.2	1,148.1 7.0	1,021.9 5.6	920.79 4.54	837.83 3.75	768.59 3.16	709.92 2.70	659.57 2.33	615.89 2.03
3	1,512.1 12.1	1,300.6 9.0	1,141.1 7.0	1,016.3 5.5	916.25 4.49	834.08 3.73	765.43 3.14	707.22 2.68	657.24 2.32	613.86 2.02
4	1,500.0 12.0	1,291.6 8.9	1,134.1 6.9	1,010.8 5.4	911.76 4.45	830.35 3.69	762.29 3.11	704.54 2.66	654.92 2.29	611.84 2.01
5	1,488.0 11.9	1,282.7 8.8	1,127.2 6.8	1,005.4 5.4	907.31 4.40	826.66 3.66	759.18 3.09	701.88 2.64	652.63 2.29	609.83 1.99
6	1,476.1 11.6	1,273.9 8.6	1,120.4 6.7	1,000.0 5.35	902.91 4.36	823.00 3.62	756.09 3.06	699.24 2.62	650.34 2.26	607.84 1.98
7	1,464.5 11.4	1,265.3 8.6	1,113.7 6.6	994.65 5.29	898.55 4.32	819.38 3.60	753.03 3.03	696.62 2.60	648.08 2.25	605.86 1.97
8	1,453.1 11.3	1,256.7 8.4	1,107.1 6.6	989.36 5.24	894.23 4.28	815.78 3.56	750.00 3.02	694.02 2.58	645.83 2.24	603.89 1.95
9	1,441.8 11.1	1,248.3 8.3	1,100.5 6.4	984.12 5.18	889.95 4.24	812.22 3.53	746.98 2.98	691.44 2.56	643.59 2.22	601.94 1.94
	1.3	1.5	1.7	1.9	2.1	2.3	2.5	2.7	2.9	3.1
0	1,430.7 10.9	1,240.0 8.3	1,094.1 6.4	978.94 5.12	885.71 4.20	808.69 3.50	744.00 2.97	688.88 2.54	641.37 2.20	600.00 1.93
1	1,419.8 10.8	1,231.7 8.1	1,087.7 6.4	973.82 5.07	881.51 4.16	805.19 3.47	741.03 2.94	686.34 2.52	639.17 2.19	598.07 1.92
2	1,409.0 10.6	1,223.6 8.0	1,081.3 6.2	968.75 5.02	877.35 4.12	801.72 3.44	738.09 2.92	683.82 2.51	636.98 2.17	596.15 1.91
3	1,398.4 10.4	1,215.6 7.9	1,075.1 6.2	963.73 4.98	873.23 4.08	798.28 3.41	735.17 2.89	681.31 2.48	634.81 2.16	594.24 1.89
4	1,388.0 10.3	1,207.7 7.7	1,068.9 6.1	958.75 4.91	869.15 4.04	794.87 3.39	732.28 2.87	678.83 2.47	632.65 2.15	592.35 1.88
5	1,377.7 10.1	1,200.0 7.7	1,062.8 6.0	953.84 4.87	865.11 4.00	791.48 3.35	729.41 2.85	676.36 2.45	630.50 2.13	590.47 1.87
6	1,367.6 10.0	1,192.3 7.6	1,056.8 6.0	948.97 4.82	861.11 3.97	788.13 3.32	726.56 2.83	673.91 2.43	628.37 2.11	588.60 1.85
7	1,357.6 9.8	1,184.7 7.5	1,050.8 5.9	944.15 4.76	857.14 3.93	784.81 3.30	723.73 2.80	671.48 2.42	626.26 2.10	586.75 1.85
8	1,347.8 9.7	1,177.2 7.4	1,044.9 5.8	939.39 4.72	853.21 3.90	781.51 3.27	720.93 2.79	669.06 2.40	624.16 2.09	584.90 1.83
9	1,338.1 9.6	1,169.8 7.3	1,039.1 5.8	934.67 4.67	849.31 3.86	778.24 3.24	718.14 2.76	666.66 2.38	622.07 2.07	583.07 1.82

The form of Table 1 is familiar and self explanatory. In Table 2, the first place of decimals is given at the head of the column, while the second place is given at the left. Between values for consecutive hundredths of degrees are given the first difference. From the table the values are 636.98 for  $\Delta = 2.92^\circ$  and 634.81 for  $\Delta = 2.93^\circ$ . By interpolation  $1860/\Delta$  for  $2.926^\circ = 636.98 - 2.17 \times 6/10 = 635.68$ , agreeing in this particular case exactly with the value calculated directly.

## THE INFLUENCE OF UNDERFEEDING AND OF SUBSEQUENT ABUNDANT FEEDING ON THE BASAL METABOLISM OF THE DOG

SERGIUS MORGULIS

All transformations taking place within the organism, concomitant with and resulting from its vital activity, are embraced under one conception of metabolism. Every living being maintains its existence by a process of combustion which involves two factors—the taking up of oxygen and setting free of carbon dioxide (and water), the amounts of which depend primarily on the degree of activity. The respiratory exchange is thus a measure of the organism's metabolic activity.

Each individual requires a certain minimum of energy to maintain its existence and under uniform conditions this minimum amount remains constant. This absolutely indispensable expenditure of energy, without which the discharge of the fundamental functions is impossible, is the organism's basal metabolism.

This basal metabolism being presumably a peculiarity of the organism, I sought to find out how it would be modified by either restricting or greatly increasing the income of combustible matter. The difficulties which one has to overcome in a study of this nature and the methods by which this has been more or less satisfactorily accomplished cannot be discussed in this preliminary note.

The subject of these experiments was a healthy and very strong Airedale dog, which had been specially trained for the experimentation. It was found that the most favorable conditions (for this dog) under which to perform respiration experiments were an external temperature of about 20–21° C. and a 24 hour fast. From several preliminary experiments it was determined that, in a state of complete restfulness and “nüchtern,” this dog consumed 4.76 liters of oxygen and expired 3.75 liters of carbon dioxide per hour. The energy equivalent of this respiratory exchange is 39.3 cal. per kilo of body weight. The dog was at this time getting a mixed



diet of meat, lard and boiled rice with an average caloric value of 70.8 cal. per kilo, or 75 per cent more than its minimum requirement. On this allowance the dog was able to just maintain a constant body weight. The average respiratory quotient, which was 0.79, indicated that the dog oxidized, for its maintenance, fat and protein primarily.

After this normal base line had been established, the diet was reduced to one-third of its former quantity, so that the animal was getting 25.7 cal. per kilo instead of 70.8 cal. In the course of the experiments its body weight diminished from 13.94 k. to 8.04 k. It is obvious that, as the weight of the dog was gradually declining, the caloric equivalent of the food supply per unit of body weight was increasing. We found that, at the close of the underfeeding, the animal was receiving 40.3 cal. per kilo. The loss of weight, however, was remarkably uniform throughout the entire experiment, following the course of a practically straight line with a constant angle of slope. During the several weeks of underfeeding a number of respiration experiments were performed at more or less regular intervals and the changes in the basal metabolism followed step by step. Within five days after the dog had been put on the insufficient diet, the gaseous exchange was found to be 3.16 liters of carbon dioxide and 4.36 liters of oxygen per hour, and a week later 3.01 and 4.03 liters respectively. Expressed in terms of energy equivalents, the basal metabolism of the dog had diminished from 546.3 cal. to 458.9 cal. per day, or over 16 per cent. From this point little change was observed in the basal metabolism, which reached a minimum of 442.4 cal. during the next five weeks. The greatest reduction in the expenditure of energy within this period was less than 6 per cent. The respiratory quotients obtained in experiments performed during that period, ranging from 0.73 to 0.76, show that fat was the material chiefly concerned in the combustion.

By this time the dog's weight had suffered a loss of over 30 per cent, and the dog showed a number of other ill effects of the underfeeding. When the first signs of physical debility had become apparent, a new abrupt change occurred in the basal metabolism of the dog. In the eighth week of underfeeding, the carbon dioxide production and oxygen consumption per hour diminished to 2.59 and 3.41 liters, respectively. During the next two weeks the gaseous



exchange speedily reached its lowest level, having diminished by fully 23 per cent, or by almost as much as it did within the previous seven weeks of underfeeding (25 per cent). The energy equivalent of the respiratory exchange was only 350.4 cal. at the end of the underfeeding experiment, whereas at the beginning it was 546.3 cal., and remained practically constant at 450 cal. during the intervening period. The respiratory quotient during the latter part of this experiment increased from 0.76 and 0.84, showing that the supply of fat in the body had been exhausted and that the dog was drawing on his protein. This inference is further sustained by the observation recorded in a former preliminary communication, that the nitrogen elimination in the urine has actually increased at the same time.

It is generally believed that, although metabolism is reduced in consequence of an insufficient supply of food, it shows no change when referred to the unit of either body weight or body surface. I cannot agree with this view, which is neither borne out by the facts of my experiments nor is it physiologically correct in its inference. By comparing the data of a number of respiration experiments, for different periods, it was found that the minimum respiratory exchange undergoes first a very marked reduction with the beginning of underfeeding but gradually increases again, and even exceeds the normal. The smallest energy requirement of the dog, per kilo, was 39.3 cal., but it was 43.6 cal., or 11 per cent more, after the dog had lost 42.35 per cent of its original weight. It is, however, preposterous to juggle with mathematical fractions, kilograms or square meters, when the subject under consideration is a biological entity. We are dealing in every instance with an organism, with an individual, and whatever its physical condition, whether well nourished or emaciated, it must be treated in its entirety. Facts disclosed by a study of the basal metabolism of convalescence give more color to this idea. On the basis of this conception the animal reacts to underfeeding as a physiological unit, and its minimum energy requirement, while continually diminishing, passes through three distinct phases: rapid decline, relative stability and, finally, renewed abrupt decline.

The essential data in this connection may be stated as follows: The average basal metabolism of a normal dog was 546.3 cal., which

was only about 2 per cent less than the highest value determined. Within ten days of deficient feeding it decreased to 458.4 cal., at which level it remained practically unaltered through a succession of weeks, the difference between the *maximum* and *minimum* values obtained during this time not exceeding 5 per cent. The second very strong diminution in the basal metabolism, during which the total energy requirement changed from 453.8 to 350.4 cal., was associated with the onset of general physical debility and more or less complete exhaustion of the material reserves of the body.

The period of abundant feeding, which followed the underfeeding, was unfortunately very brief, but the results of six respiration experiments performed during that time are extremely interesting. When the data are published in full a number of facts will be stated pertaining to this period of recuperation which cannot be mentioned here for want of space. Suffice it to say that at the close of four weeks of liberal realimentation, the original weight had been restored while the general physical condition of the animal had returned to its normal level. The diet during this time, considering its caloric value, had been superabundant—was about 200–300 per cent over and above the lowest requirement. The respiratory exchange gradually rose from 2.54 liters of carbon dioxide and 3.01 liters of oxygen, per hour, to 4.72 and 6.31 liters respectively, in two weeks. This increase in the gaseous metabolism, which represents an increase of over 100 per cent in terms of energy production, had then reached its climax, and was accompanied by a most vigorous process of upbuilding.

*Although the supply of nourishment still remained excessive, the gaseous metabolism began to diminish at this stage and in the course of the next two weeks attained practically the same intensity which the normal animal had displayed in the preliminary investigation.* Thus, the carbon dioxide production per hour became 3.89 liters and the oxygen consumption 5.21 liters (3.75 and 4.76 liters respectively during the preliminary period). The rate of respiration and pulsation, as well as the body temperature, meanwhile also became absolutely normal. There had been no adaptation on the part of the organism to the greater inflow of energy. Its metabolic activity had been temporarily raised while the exhausted organs and tissues had been rapidly repaired, but as soon as the storing away of re-

serves predominated over the constructive processes, the basal metabolism went back to its original level, the level which was characteristic for this particular organism.

Our dog responded to the vicissitudes of experimentation not as a mosaic of kilograms, but as a physiological entity tending to retain or to restore its organic equilibration.

*College of Physicians and Surgeons,  
Columbia University*

## THE NINHYDRIN REACTION

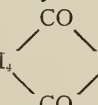
PAUL E. HOWE

The recent use of the characteristic reaction between triketohydrindene hydrate (ninhydrin) and amino acids, peptones, etc. (blue coloration), for the detection of products of protein hydrolysis in tests for pregnancy,<sup>1</sup> and its further application to other tests, have elicited considerable interest in the nature of the reaction, the limits of its applicability, and the factors which may modify its sensitiveness. Ruhemann<sup>2</sup> has studied this reaction carefully and was the first<sup>3</sup> to prepare triketohydrindene hydrate in sufficient quantity to analyze it, and to determine its chemical and physical properties.<sup>4</sup> He recognized the characteristic reaction with amino

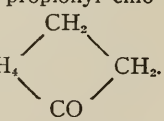
<sup>1</sup> Abderhalden: *Münch. med. Woch.*, 1912, lix, p. 1939.

<sup>2</sup> Ruhemann: *Jour. Chem. Soc. Trans.*, 1910, xcvi, pp. 1438 and 2025; *ibid.*, 1911, xcix, p. 792; *ibid.*, 1912, ci, p. 780.

<sup>3</sup> Beilstein mentions triketohydrindene in his third edition, Vol. iii, p. 314 (1897), and in the subsequent "Aufgangs Band," iii, p. 242, mentions the method of preparation outlined by Kaufmann (B. 1897, xxx, p. 387), who could not obtain sufficient material to make an analysis.

<sup>4</sup> Triketohydrindene hydrate,  $\text{C}_6\text{H}_4$   crystallizes from water

in colorless prisms, which on heating lose water and at 125° C. turn red, froth at 139° C. and melt at 239-240° C. The compound is moderately soluble in cold water, readily so in hot water, sparingly soluble in ether, and quite readily soluble in ethyl acetate. It is decomposed by ammonium compounds, yielding scarlet prisms, reduces Fehling sol. and ammoniacal silver nitrate sol., and forms hydrazones and addition compounds. (Ruhemann.)

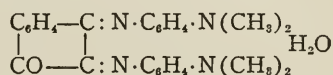
Triketohydrindene hydrate can be prepared from cinnamic acid through a series of reactions involving its reduction, chlorination (phenyl-propionyl chlorid) and the removal of hydrochloric acid, giving  $\alpha$ -hydrindone  $\text{C}_6\text{H}_4$  .

(Kipping: *Jour. Chem. Soc. Trans.*, 1894, lxv, p. 48.) This latter compound, when treated with *p*-nitrosodimethylanilin (Ruhemann: *loc. cit.*), in the presence

acids and realized its importance to biological chemistry. As a result of his researches, Ruhemann showed that the reaction between triketohydrindene hydrate and the amino acids depends upon the presence of free, intact, amino and carboxyl groups which are attached either to an aliphatic compound (radical) or to the aliphatic side chain of an aromatic compound. The amino group may be either in the  $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$  or  $\epsilon$ , position although the  $\alpha$ -compounds are the most reactive; the other compounds usually require the application of heat to produce a color. The formation of the color substance is associated with the production of an aldehyde. Tests with a number of amino acids and other biological products<sup>5</sup> have shown that the *blue* reaction is given by compounds having the groups indicated above.<sup>6</sup>

It has been noted (Ruhemann) that a blue coloration results when a solution of triketohydrindene hydrate is warmed in strongly alkaline solutions; upon dilution the color disappears, or with dilute alkalis the reaction is obtained only with difficulty. Subsequently<sup>7</sup> it was shown that conc. solutions of alcohols, aldehydes, ketones and reducing sugars give the red or blue coloration when warmed with triketohydrindene hydrate, which is intensified by the addition of alkali. Dilution here, as with the alkalis, resulted in the dissipation of the color. The colored products obtained with these substances under the conditions outlined above, are not the same as those formed with amino acids.

of alcoholic potassium hydroxid sol., gives a substitution product—the hydrate of 2:3-bis (*p*-dimethylaminoanilo)  $\alpha$ -hydrindone,



which, when warmed slightly with dilute sulfuric acid, gives triketohydrindene hydrate.

<sup>5</sup> Ruhemann: *Loc. cit.*; Abderhalden and Schmidt: *Zeit. f. physiol. Chem.*, 1911, lxxii, p. 37.

<sup>6</sup> Ruhemann found that one part of triketohydrindene hydrate in 15,000 of water gives a reaction with glycolol, while the same dilution gives a yellow coloration with ammonia—ordinarily, red to reddish yellow in more concentrated solutions. Abderhalden and Schmidt found that, when 0.1 gm. of the substance is dissolved in 30 c.c. of water and 0.1 c.c. of this is taken, glycolol gives a distinct reaction in dilutions of 1:10,000, alanin a sharp reaction at 1:10,000 and *l*-tyrosin at 1:5,000.

<sup>7</sup> Halle, Loewenstein and Pribram: *Biochem. Zeit.*, 1913, lv, p. 357.



A study<sup>8</sup> of the factors which may interfere with the reaction has shown that the solutions involved must be neutral. A more detailed consideration<sup>9</sup> of the factors which influence the production of the blue color has shown that the addition of alkali to the solution to be tested, before the addition of the triketohydrindene hydrate, interferes with the test; the addition of alkali after the color has developed does not dissipate the color. Acids, even comparatively weak organic acids, not only hinder the reaction but decolorize the solution after the color has developed. The effect of the higher fatty acids depends upon whether they are saturated or unsaturated, in the latter case they interfere. The effect of electrolytes varies with the cation and is independent of the anion. In some cases (sodium and potassium) there is a precipitation of the colloidal color substance, in other cases (calcium and cadmium) the effect is a change in the intensity of the color without precipitation, while in still others (ammonium and magnesium) there is no appreciable change.

A few observations upon the biological activity of triketohydrindene hydrate have shown that following hypodermic injection (frogs) the tissues are stained blue and cardiac paralysis results. The fatal dose for frogs is 0.002–0.005 gm. and death may ensue without the appearance of the substance in the urine. It is an irritant poison, a 1/1024 percent solution causing a transitory burning sensation when dropped on the eye. It is not a general protoplasmic poison, for the growth of yeast is hardly inhibited.

From the evidence cited it appears that triketohydrindene hydrate (ninhydrin) is a very satisfactory test for the presence of compounds having free amino and carboxyl groups attached to aliphatic radicals—amino acids, peptone, protein, etc. The typical blue color may result under other conditions than in the presence of amino acids and the related substances. When the reagent is used under the conditions ordinarily prescribed—in a neutral solution, distilled water with a negative or very low salt content—a positive test results only in the presence of amino acids.

*Biochemical Laboratory of Columbia University,  
College of Physicians and Surgeons, New York*

<sup>8</sup> Ruhemann: *Loc. cit.*; Abderhalden and Schmidt: *Loc. cit.*

<sup>9</sup> Halle, Loewenstein and Pribram: *Loc. cit.*

## A RAPID CLINICAL TEST FOR HYPERGLYCEMIA

S. GITLOW AND B. HOROWITZ

(*Biochemical Laboratory, Fordham University Medical School, New York City*)

The purpose of this investigation was to devise a rapid clinical method for the detection of hyperglycemia—a method which could be applied by the practising physician as readily as he applies Fehling's. As it was desirable to make the test applicable to very small quantities of blood, a delicate colorimetric test for carbohydrate was considered. The one selected was Molisch's.

As we were desirous of establishing a definite relationship between concentration and intensity of coloration, the usual method of carrying out the Molisch test, namely, by ring formation, was ignored; instead, coloration of the solution after mixing the reagents was alone considered.

The difficulties at the outset were those of getting controls that would show no coloration. In spite of an exhaustive examination into the purity of the reagents employed (sulfuric acid, water,  $\alpha$ -naphthol, and alcohol) and attempts to substitute other reagents, such as thymol for  $\alpha$ -naphthol and chloroform for alcohol, the results were not very satisfactory. Particular attention was paid to the cleanliness of the test tubes employed.

Other workers in the field have also experienced difficulties of this nature. Oppenheimer advises the use of a *colorless* saturated solution of  $\alpha$ -naphthol, which means that fresh solutions would have to be prepared repeatedly. In our own experience this was not found to offer any particular advantage. Udranzky emphasizes the importance of clean test tubes, and the advisability of purifying the alcohol with animal charcoal before use. Dust particles he found especially troublesome. With the exception of purification of the alcohol, these directions are important. Luther's observation that chloroform is an effective substitute for alcohol is not in accordance with our own findings.

In spite of the difficulty of getting perfect colorless controls, the method was further studied in an attempt to utilize it for comparative tests, as for example, in the comparison of the color of a standard sugar solution which had been treated with the Molisch reagents with that of blood treated similarly; or the differentiation of normal from diabetic urine. Whilst it is true that the intensity of the coloration is proportional to the concentration of the carbohydrate, and that the element of time is a factor that cannot be neglected, two other important points have to be considered: the order in which the reagents are mixed, and the amount of water present. The reagents are best added in the following order:  $\alpha$ -naphthol, solution to be tested (or vice versa), water, sulfuric acid. As heat accelerates the velocity of the reaction, and water and sulfuric acid produce heat, it is evident that the amount of water added (as well as that of sulfuric acid) must be the same throughout.

Several kinds of blood have been tested: Guinea pig (ear lobe) and human (apparently normal, also made artificially hyperglycemic by the addition of glucose, and diabetic). The guinea-pig blood was diluted with ten volumes of water. A series of tests was made containing successively 1, 2, 3, 4, 5, 6, 7, 8, 9 drops of this diluted blood in test tubes. Controls with no blood, one with no  $\alpha$ -naphthol and a sugar control were made, thus:

Number of the test	1	2	3	4	5	6	7	8	9	10	11	12
Diluted blood (drops).....	—	1	2	3	4	5	6	7	8	9	9	—
$\alpha$ -naphthol sol. (drops).....	1	1	1	1	1	1	1	1	1	1	1	1
Water (drops).....	4	13	12	11	10	9	8	7	6	5	5	14
Sulfuric acid sol. (c.c.).....	2	2	2	2	2	2	2	2	2	2	2	2
Glucose sol.—1 : 100 (drop).....	—	—	—	—	—	—	—	—	—	—	—	1

Control 1 gave no pink color. Control 11 gave a green color, which changed to light brown with the addition of more blood. The intensity of the pink color increased with the quantity of the blood taken. The color of the sugar control (12) corresponded with the color between 2 and 3. This corresponds to a dilution of 0.1 per cent of glucose. The addition of sugar (1-100 sol.) to the blood intensifies the color proportionately.

Two c.c. of sulfuric acid solution had to be used with the blood

in the proportions employed because 1 c.c. was not sufficient to give a clear solution. The addition of the extra c.c. of sulfuric acid sol. removed this difficulty.

Equally satisfactory results were gotten with diluted normal human blood, artificial hyperglycemic human blood and diabetic blood. The blood was made artificially hyperglycemic by the addition of sufficient glucose to make the proportion 0.2 per cent. The difference between the normal and the two hyperglycemic bloods, in their response to the test, was very marked with the use of 1 drop of the diluted blood, more marked with 2 drops.

An attempt was made to compare the responses to the test by blood with those by sugar. This was found to be impossible because the color produced by blood is different from that caused by a sugar solution. By substituting serum for blood, the colored solutions obtained with the Molisch reagents approximated far more nearly to that obtained with a pure sugar solution. In this way, by comparison with standard sugar solutions, quantitative measurements were undertaken. However, the results were invariably high (0.1–0.2 per cent for normal, and from 0.3 per cent up for hyperglycemic samples). This may be attributed, in part at least, to the serum proteins, for, as is well known, proteins give a positive Molisch test. Quantitative estimations, after removal of the proteins, are now being attempted.

*Conclusion.* The Molisch test is available for the detection of sugar in blood. The difference in color between tests performed on normal and hyperglycemic bloods is very marked and very readily detected.

## THE AGRICULTURAL COLLEGES AND EXPERIMENT STATIONS IN THE UNITED STATES\*

Officers of the Association of American Agricultural Colleges and Experiment Stations, 1914. Pres't: *A. C. True*, Washington, D. C.; vice-pres'ts: *J. M. Hamilton*, Mont., *J. F. Duggar*, Ala., *Alva Agee*, N. J., *K. L. Butterfield*, Mass., *R. A. Pearson*, Ia.; sec'y-treas.: *J. L. Hills*, Vt.; bibliographer: *A. C. True*; exec. commit.: *W. O. Thompson*, O., chairman; *H. J. Waters*, Kan., *Brown Ayres*, Tenn., *W. H. Jordan*, N. Y., *H. L. Russell*, Wis.

SECTIONS.—COLLEGE WORK AND ADMINISTRATION: *E. D. Sanderson*, W. Va., chairman; *C. A. Lory*, Col., sec'y. Commit. on program: chairman and sec'y. EXPERIMENT STATION WORK: *J. G. Lipman*, N. J., chairman; *E. A. Burnett*, Neb., sec'y; *W. H. Beal*, Washington, D. C., recording sec'y. Commit. on program: chairman, sec'y and recording sec'y. EXTENSION WORK: *W. D. Hurd*, Mass., chairman; *E. G. Peterson*, Utah, sec'y; *John Hamilton*, Pa., recording sec'y. Committee on program: chairman and sec'y.

STANDING COMMITTEES.—INSTRUCTION IN AGRICULTURE: Three years, *H. J. Waters*; *A. C. Monahan*, Washington, D. C.; two years, *J. F. Duggar*, Ala., and *W. H. French*, Mich.; one year, *A. C. True*, chairman, and *T. F. Hunt*, Cal. GRADUATE STUDY: Three years, *F. B. Mumford*, Mo., and *H. J. Webber*, Cal.; two years, *W. O. Thompson*, O., and *Brown Ayres*; one year, *H. P. Armsby*, Pa., chairman, and *Howard Edwards*. EXTENSION WORK: Three years, *G. I. Christie*, Ind., and *W. J. Kennedy*, Ia.; two years, *Alva Agee*, *C. W. Pugsley*, Neb., chairman; one year, *W. D. Hurd* and *H. L. Russell*. EXPERIMENT STATION ORGANIZATION AND POLICY: Three years: *F. B. Linfield*, Mont., and *C. E. Thorne*, O.; two years, *E. W. Allen*, Washington, D. C., and *B. W. Kilgore*, N. C.; one year, *Eugene Davenport*, Ill., chairman, and *C. D. Woods*, Me. COLLEGE ORGANIZATION AND POLICY: Three years, *R. A. Pearson*, *A. R. Hill*, Mo.; two years, *J. M. Hamilton*, *K. L. Butterfield*, chairman; one year, *Samuel Avery*, Neb., and *W. M. Riggs*, S. C.

Officers and committees of the American Association of Farmers' Institute Workers, 1914. Pres't: *Edward Van Alstyne*, Albany, N. Y.; vice-pres't: *W. J. Black*, Winnepeg, Can.; sec'y-treas.: *L. R. Taft*, East Lansing, Mich.; honorary sec'y: *John Hamilton*, State College, Pa.; executive commit.: pres't and sec'y-treas., ex-officio; *A. L. Martin*, Harrisburg, Pa., chairman; *T. B. Parker*, Raleigh, N. C.; *Mrs. F. L. Stevens*, Mayaguez, Porto Rico.

A. C.

\* Continued from the October issue: BIOCHEM. BULL., 1913, iii, p. 102.



PROCEEDINGS OF THE FIRST ANNUAL MEETING OF  
THE FEDERATION OF AMERICAN SOCIETIES  
FOR EXPERIMENTAL BIOLOGY, IN  
PHILADELPHIA, DEC. 28-31, 1913<sup>1</sup>

PAUL E. HOWE

PREPARED FROM REPORTS BY THE SECRETARIES OF THE CONSTITUENT SOCIETIES,  
A. J. CARLSON, P. A. SHAFFER, JOHN AUER AND G. H. WHIPPLE

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I. GENERAL COMMENT ON THE FEDERATION OF AMERICAN  
SOCIETIES FOR EXPERIMENTAL BIOLOGY

A

A. J. Carlson,

Secretary of the Executive Committee for 1913

For a number of years the members of the Physiological, Biochemical and Pharmacological Societies have felt the desirability of a closer co-operation of these and other biological societies, especially as regards the annual scientific meetings. At the meeting in Chicago, in 1907, the Physiological Society appointed a committee on policy, with instructions to report at the next annual meeting. At the meeting in Baltimore, in 1908, the chairman of this committee, Dr. A. P. Mathews, presented a plan for reorganizing all the existing biological societies into a general biological society. The

<sup>1</sup> For a report of the organization of the Federation see Auer: *BIOCHEM. BULL.*, 1913, ii, p. 269.

plan involved a change in policy and in the character of the membership of at least some of the societies, and an extensive venture in the publication of scientific journals. These features were not endorsed by the society, but the general plan of affiliation of all the biological societies was favorably received and Dr. Mathews was appointed delegate from the Physiological Society to confer with delegates from the other biological societies to this end. This committee does not appear to have made any progress.<sup>2</sup>

At the meeting in Cleveland, in 1912, the Physiological, Biochemical and Pharmacological Societies appointed committees to propose plans for affiliation. The committee consisted of Drs. Meltzer, Lee and Cannon from the Physiological Society, Drs. Lusk and Wells from the Biochemical Society,<sup>3</sup> and Drs. Sollmann, Loevenhart and Auer from the Pharmacological Society. This committee submitted the following plan:

That the three societies affiliate under the name of the Federation of American Societies for Experimental Biology.

That the president and secretary of each of the three societies constitute collectively the executive committee of the Federation.

That programs of the annual meetings be printed under one cover, and that the secretaries confer and adjust the papers with a view of effecting the greatest co-ordination.

That meeting places in common, for the Federation and the societies of anatomists, zoologists and naturalists, are desirable.

The first annual meeting in Philadelphia, Dec. 28-31, 1913, was arranged by the executive committee of the Federation according to the above plan. Those present at the meeting were in substantial agreement that it was a success. *At this meeting the plan of the organization committee was ratified by the three societies and the American Society for Experimental Pathology joined the Federation.* This brings the total membership of the Federation up to about 450.

The distinctive feature of the Federation plan is the co-operation

<sup>2</sup> Further editorial comment on the organization of the Federation is published on page 337 of this issue.

<sup>3</sup> The Biochemical Society was represented by only two members, because the third representative, Dr. Gies, though an advocate for some years of the formation of a federation, was unavoidably absent from the Cleveland meeting. *BIOCHEM. BULL.*, 1913, ii, p. 269. [Ed.]

and co-ordination in the essential things, with no interference with the individuality of the constituent societies. This co-operation is certainly desirable between all the biological societies, and we believe the Federation plan can and ought to be extended in that direction. We believe it will increase the efficiency of the societies as agencies for the promotion of research and dissemination of truth.

At the first executive meeting of the Federation, Dec. 31, 1913, the following declaration on the subject of animal experimentation was unanimously adopted:

(1) We, the members of the Federation of American Societies for Experimental Biology—comprising the American Physiological Society, the American Society of Biological Chemists, the American Society for Pharmacology and Experimental Therapeutics, and the American Society for Experimental Pathology—in convention assembled, hereby express our accord with the declaration of the recent International Medical Congress and other authoritative medical organizations, in favor of the scientific method designated properly animal experimentation but sometimes “vivisection.”

(2) We point to the remarkable and innumerable achievements, by means of animal experimentation in the past, in advancing the knowledge of biological laws; and devising methods of procedure for the cure of disease, and for the prevention of suffering in human beings and lower animals. We emphasize the necessity of animal experimentation in continuing similar beneficent work in the future.

(3) We are firmly opposed to cruelty to animals. We heartily support all humane efforts to prevent the wanton infliction of pain. The vast majority of experiments on animals need not be and, in fact, are not accompanied by any pain whatsoever. Under the regulations already in force, which reduce discomfort to the least possible amount and which require the decision of doubtful cases by the responsible laboratory director, the performance of those rare experiments which involve pain is, we believe, justifiable.

(4) We regret the widespread lack of information regarding the aims, the achievements and procedures of animal experimentation. We deplore the persistent misrepresentation of these aims, achievements and procedures by those who are opposed to this scientific method. We protest against the frequent denunciations of self-sacrificing, high-minded men of science, who are devoting their lives to the welfare of mankind in efforts to solve the complicated problems of living beings and their diseases.

## B

John Auer,

Secretary of the Pharmacological Society

As the reader probably remembers, the Federation of the American Societies for Experimental Biology was formed provisionally in Cleveland, at a meeting of duly appointed delegates from the Physiological, Biochemical and Pharmacological Societies. The recommendations of this conference committee<sup>4</sup> were submitted by the delegates to the members of the three societies during the 1913 session in Philadelphia and the recommendations were adopted in full: *Et factus est federatio in animam viventem*.

There was some informal discussion about the necessity of elaborating rules for the guidance of Federation affairs, but there was no tendency to act precipitately. It was fully realized that caution was necessary, first, in order to avoid collision with the several constitutions of the constituent societies and, secondly, in order that the fullest individual freedom of the component societies might be maintained. No attempt was made, therefore, to constrict the three societies by the hoop of a federal constitution, but some motions were passed which will tend to preserve and emphasize the unity of the Federation. Thus, not only will the annual programs of the constituent societies of the Federation be published under one cover, but the membership lists and constitutions also. This promises to be a great convenience, for many men are members of at least three of the societies, and now receive at least four<sup>5</sup> separate pamphlets, some of which are sure not to be at hand when wanted.

Another regulation was one designed to aid in the administration of the Federation affairs if the chairman and secretary of the executive committee<sup>6</sup> should be retired. The motion provides that

<sup>4</sup> The minutes of this conference committee were published in full in the *BIOCHEM. BULL.*, 1913, ii, p. 269.

<sup>5</sup> The Pharmacologists, for example, publish their membership list and constitution separately.

<sup>6</sup> The reader may recollect that the president and secretary of the presiding society are chairman and secretary, respectively, of the executive committee of the Federation. The societies preside regularly in this rotation: Physiological Biochemical, Pharmacological, Pathological.



the chairman and secretary of the executive committee, in the event of retirement from office in their society, become members of the executive committee for the ensuing year but in an *advisory* capacity only. The committee will thus always enjoy the advice of the chairman and secretary of the preceding year, but there is no danger that one society will have at its disposal four votes out of ten in the deliberations of the executive committee of the Federation.

An illustration of the independence of the societies forming the Federation is furnished by an action of the Pharmacological Society. This society has a constitutional provision which renders those in the permanent employ of drug firms ineligible to membership. As the other societies have no such clause, it was easily conceivable that the spirit of this clause might be violated by the shifting of papers from one society to another on the annual program, which the Federation authorizes. In order to emphasize again its own individual position in this matter, and to prevent the possible appearance of papers from commercial interests on its programs, the society passed a resolution recommending that no paper should be transferred to its program without the explicit consent of the secretary of the Pharmacological Society.

An action of this kind shows quite well that the individuality of a society belonging to the Federation is preserved, and that the Federation itself is merely a working combination, a loose chemical union, so to say, designed to concentrate the kinetic energy of the individual molecule-societies on one point, in the furtherance of a proper experimental attitude in the biological sciences. Moreover, this loose combination between the components of the Federation is a guarantee that a cleavage of the Federation by the secession of a society desirous of satisfying some more attractive affinity, will be accompanied by a minimal liberation of heat and evolution of gas.

## II. SCIENTIFIC PROGRAMS OF THE GENERAL SESSIONS OF THE FEDERATION

A. J. Carlson,

Secretary of the Executive Committee for 1913

First session. Jefferson Medical College, Monday, December 29, 9.00 a. m. PRESIDING OFFICER: *President of the Physio-*



*logical Society and Chairman of the Executive Committee of the Federation for 1913, S. J. Meltzer.*

*S. J. Meltzer:* Presidential address, on The theories of anesthesia.—*Graham Lusk:* Phlorhizin glycosuria before and after thyroidectomy.—*A. J. Ringer and E. M. Frankel:* Studies in diabetes, (a) The effect of different compounds on glycogenesis; (b) The mechanism of antiketogenesis.—*L. B. Mendel and T. B. Osborne:* Some problems of growth, (a) The capacity to grow; (b) The role of amino acids in growth.—*Andrew Hunter:* Further studies in the comparative biochemistry of purin metabolism.—*W. R. Bloor:* Changes in fats during absorption.—*Leo Loeb:* Immunization against the anti-coagulating effect of leech extract.—*C. W. Edmunds:* Anaphylaxis in the cat and opossum.—*J. J. Abel, L. S. Rowntree and B. B. Turner:* Vividiffusion; report on preliminary results.—*C. L. von Hess and H. McGuigan:* A method of dialysing normal circulating blood and some of its applications.—*A. Woelfel and A. L. Tatum:* A biological test for iodine in the blood.—*L. G. Henderson and W. W. Palmer:* Further studies of the excretion of acids.

**Second session.** University of Pennsylvania, Tuesday, December 30, 2.00 p. m. **PRESIDING OFFICER:** *President of the Physiological Society and Chairman of the Executive Committee of the Federation for 1913, S. J. Meltzer.*

**DEMONSTRATIONS.** *R. G. Pearce:* The influence of the vagi on renal secretion.—*F. H. Pike:* Stimulation of the semi-circular canals.—*J. J. Abel, L. G. Rowntree and B. B. Turner:* Demonstration of vividiffusion.—*P. A. Shaffer:* The determination of blood sugar.—*F. R. Miller:* Intestinal peristalsis in *Homarus*.—*C. Brooks:* Methods for studying the pharmacology of the circulation.—*C. J. Wiggers:* The contour of the intraventricular and the pulmonary arterial-pressure curves by two optically recording manometers.—*C. C. Guthrie:* Some time-saving laboratory methods.—*W. B. Cannon and W. L. Mendenhall:* A graphic method for recording the coagulation of blood.—*F. L. Gates and S. J. Meltzer:* Some mutual relations of oxalates, salts of magnesium and calcium; their concurrent and antagonistic actions.—*A. J. Carlson:* A method of obtaining successive contrast of the sensations of hunger and appetite.—*S. Simpson:* Further observations on the pyramidal tracts of the

raccoon and porcupine.—*A. Woelfel*: A new apparatus for demonstration of the dioptrics of the eye and the principles of ophthalmoscopy and retinoscopy.—*Y. Henderson*: Simple experiments on respiration for the use of students.—*R. D. Hooker*: Convenient modification for venous pressure determinations in man.—*R. A. Gesell* and *J. Erlanger*: Device for interrupting a continuous blast of air, designed especially for artificial respiration.—*C. W. Edmunds*: A simple liver plethysmograph.—*W. P. Lombard*: An artificial circulation apparatus for students.—*H. H. Bunzel*: A simplified and inexpensive oxidase apparatus.—*M. Dresbach*: An improved form of apparatus for perfusion of the excised mammalian heart.

### III. AMERICAN PHYSIOLOGICAL SOCIETY: TWENTY-SIXTH ANNUAL MEETING

A. J. Carlson, Secretary

The twenty-sixth annual meeting of the American Physiological Society was held at the University of Pennsylvania and at the Jefferson Medical College, December 28–31, 1913. One hundred and eighteen of the members of the Society were present at the meeting. This, the largest, attendance in the history of the society was due, in part, to the fact that the societies representing the biochemists, pharmacologists, pathologists, anatomists, zoologists, and naturalists met in Philadelphia at the same time. This is a most excellent plan, and should be made a fixed policy of the biological societies. The members of all the biological societies had joint dinners and smokers the three evenings of the meeting.

Two of the scientific sessions of the Physiological Society were joint meetings with the Biochemical and Pharmacological Societies. The scientific program was as usual a lengthy one and comprised a number of papers of unusual importance. The number and general high grade of the demonstrations was also a feature of the meeting.

**Scientific program.** FIRST SESSION. JEFFERSON MEDICAL COLLEGE, MONDAY, DECEMBER 29, 2.00 P. M. *T. F. Zucker*: Studies on blood plates.—*W. H. Howell*: The condition of the blood in hemophilia.—*W. B. Cannon* and *W. L. Mendenhall*: Some physiological factors affecting the coagulation time of blood.—*J. A. E.*

*Eyster*: The action of epinephrin on the heart.—*P. G. Stiles* and *E. G. Martin*: Two types of reflex fall of blood pressure.—*A. W. Hewlett*: Dicrotism and the brachial-flow pulse.—*Jessie L. King*: The periodic cardio-vascular and temperature variations in women.—*H. S. Gasser* and *W. J. Meek*: Acceleration of the heart in exercise.—*R. G. Hoskins* and *H. Wheelon*: On the constancy of blood pressure and vaso-motor reactions in the anesthetized dog.—*A. L. Prince*: The relative systolic discharges of the left and right ventricles.—*W. J. Meek* and *J. A. E. Eyster*: The effect of vagal stimulation on the location of the pace-maker of the mammalian heart.—*R. A. Gesell*: The effect of pulsation on filtration.—*F. C. Becht*: The action of pilocarpin on the cerebrospinal fluid.

SECOND SESSION. UNIVERSITY OF PENNSYLVANIA, TUESDAY, DECEMBER 30, 9.00 A. M. *E. B. Meigs*: The osmotic properties of clam muscle.—*W. N. Berg*: (a) Sources of surface tension in striated muscle; (b) Maximum surface tension in striated muscle.—*F. S. Lee*: Some characteristics of mammalian muscle.—*E. G. Martin*: Some results obtained by the use of quantitative faradic stimuli in physiological investigation.—*J. Erlanger* and *W. E. Garrey*: Faradic stimuli; A physical and physiological study.—*S. Tashiro*: (a) The metabolic gradient in the nerve fibre; (b) The action of anesthetics on carbon-dioxid production in the nerve fibre.—*A. C. Crehore* and *H. B. Williams*: Proof that the propagation of the nervous impulse obeys the laws of propagation of electricity along conductors with distributed capacity.—*R. D. Hooker* and *S. O. Reese*: Saline perfusion of the spinal centres in frogs; The effect of calcium and potassium chloride.—*H. C. Jackson* and *E. M. Ewing*: Variations in the reflex responses through medullary centres.—*E. L. Mellus*: Evidences in the cerebral cortex of mental equipment and intellectual development.—*P. W. Cobb*: The influence of surroundings on foveal vision.—*E. L. Porter*: The effect of strychnin on reflex thresholds.

THIRD SESSION. UNIVERSITY OF PENNSYLVANIA, WEDNESDAY, DECEMBER 31, 9.00 A. M. *J. J. R. Macleod* and *R. G. Pearce*: Sugar consumption in eviscerated animals.—*I. S. Kleiner* and *S. J. Meltzer*: On the rapid disappearance from the blood of large quantities of dextrose injected intravenously.—*J. R. Murlin*: Further observations on the metabolism of depancreatized dogs.—*R. T.*

*Woodyatt* and *B. O. Raulston*: Transfusion of blood in severe diabetes mellitus.—*A. B. Luckhardt*: The cause of diabetic polyphagia.—*E. F. DuBois*: Preliminary report on work with a respiration calorimeter in Bellevue Hospital.—*W. E. Burge*: The role of nascent oxygen in protecting the body from self-digestion.—*A. E. Livingston*: The effect of castration on the hypophysis in the rabbit.—*R. W. Keeton*: The secretion of gastric juice during parathyroid tetany.—*G. W. Crile*: The brain-adrenal-thyroid-liver-pancreas syndrome (kinetic system).—*T. L. Patterson*: The variations in the hunger contractions of the empty stomach with age.—*A. J. Carlson*: The control of the hunger mechanism.

**Executive proceedings.** ORGANIZATION OF THE FEDERATION. The most important matter in the way of business was the ratification of the work of the conference committee, appointed at the Cleveland meeting, establishing the Federation of American Societies for Experimental Biology. One of the aims of this Federation is the coordination of the scientific work at the annual meetings, a successful beginning of which was made this year. A great deal of the credit for this successful beginning is due to the splendid facilities offered by the Philadelphia institutions, and the careful planning and hard work of the local committee.

NEW MEMBERS: *E. F. DuBois*, Cornell Univ. Med. Coll.; *E. M. Ewing*, N. Y. Univ. and Bellevue Hosp. Med. Coll.; *G. Fahr*, Johns Hopkins Med. Sch.; *Mabel P. FitzGerald*, N. Y. City; *R. E. Gesell*, Washington Univ.; *O. C. Glaser*, Univ. of Mich.; *P. E. Howe*, Columbia Univ.; *J. H. King*, Johns Hopkins Med. Sch.; *E. Ladholz*, Univ. of Penn.; *H. Laurens*, Yale Univ.; *H. A. Mattill*, Univ. of Utah; *E. L. Porter*, Harvard Med. Sch.; *O. O. Stoland*, Univ. of S. Dak.; *J. E. Sweet*, Univ. of Penn.; *S. Tashiro*, Univ. of Chicago; *A. L. Tatum*, Univ. of Chicago. The total membership of the Society is now 210.

NEXT MEETING. Washington University presented an invitation to meet in St. Louis next year. The Society voted in favor of meeting in St. Louis, but the final decision is left with the Executive Committee of the Federation.

AMER. JOURN. OF PHYSIOL. The editorial committee (Drs. Porter, Carlson, Erlanger, Howell, Lee, Lusk, Macallum) was instructed by the Society to report at the next annual meeting on the



relation of the *American Journal of Physiology* to the American Physiological Society and to propose measures to improve the facilities for publication on the part of American Physiologists.

OFFICERS-ELECT: President—*W. B. Cannon*; Secretary—*A. J. Carlson*; Treasurer—*J. Erlanger*; Additional members of the Council—*F. S. Lee, S. J. Meltzer*.

#### IV. THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS: EIGHTH ANNUAL MEETING

P. A. Shaffer, Secretary

The eighth annual meeting of the American Society of Biological Chemists was held at Philadelphia on December 29–31, 1913, in affiliation with the American Physiological Society, and the American Society for Pharmacology and Experimental Therapeutics, as the Federation of American Societies for Experimental Biology. The meetings of the Society were well attended and highly successful. The joint meetings, as in past years, were of great interest to the members of all of the societies, and these, together with the co-operation in the arrangement and printing of programs, emphasized the advantages of the closer relations between the societies made permanent by the formation of the Federation. The scientific program is appended.

**Scientific program.** FIRST SESSION. JEFFERSON MEDICAL COLLEGE, MONDAY, DECEMBER 29, 2.30 P. M. *A. B. Macallum*: Presidential address, on Some problems in cellular physics and chemistry.—*H. G. Wells* and *T. B. Osborne*: The so-called vegetable proteoses and their biological reactions.—*H. C. Bradley*: Some anaphylactic reactions.—*D. D. Van Slyke* and *G. E. Cullen*: The mode of action of soy-bean urease.—*R. T. Woodyatt*: Glycol aldehyde in phlorhizined dogs.—*P. A. Kober* and *S. S. Graves*: Trikresol as a substitute for toluene in enzyme work.—*J. C. Da-Costa, E. H. Funk, O. Bergeim* and *P. B. Hawk*: A study of the metabolism in *Osteitis deformans*.—*S. Bookman*: Metabolism in *Diabetes insipidus*.—*H. I. Mattill* and *H. A. Mattill*: Some metabolic effects of bathing in Great Salt Lake.—*W. H. Park, E. J. Banzhaf* and *L. W. Famulener*: Absorption of antitoxin from solutions containing different percentages of protein.



SECOND SESSION. UNIVERSITY OF PENNSYLVANIA, TUESDAY, DECEMBER 30, 9.00 A. M. *A. W. Peters* and *M. E. Turnbull*: The carbohydrate tolerance of feeble-minded children especially of the Mongolian type.—*A. I. Ringer* and *G. W. Raiziss*: Protein metabolism in individuals with exfoliative conditions of the skin.—*P. H. Mitchell*: The oxygen requirements of shell fish.—*W. McK. Marriott*: The metabolic relationship of the acetone substances.—*E. D. Clark* and *R. A. Gortner*: Phenomena of narcosis of leaves of the wild indigo (*Baptisia tinctoria*) and consequent production of a new phenol.—*A. B. Macallum* and *J. B. Collip*: A hitherto unknown constituent of nerve cells.—*H. M. Adler* and *B. H. Ragle*: A note on the chemical constituents of the cerebrospinal fluid in certain cases of insanity.—*A. E. Taylor* and *C. W. Miller*: On the estimation of minute quantities of phosphorus.—*I. Greenwald*: Formation of glucose from citric acid in *Diabetes mellitus* and in phlorhizin glycosuria.—*J. P. Atkinson*: Further results upon the electrolysis of peptids and amino acids.—*George Peirce*: Researches on the heptoses.—*C. G. Fawcett* and *J. A. Rahe*: The nerve control of the thyroid gland.

THIRD SESSION. UNIVERSITY OF PENNSYLVANIA, WEDNESDAY, DECEMBER 31, 9.00 A. M. *H. H. Bunzel*: Biological oxidizability and chemical constitution.—*J. L. Hydrich*: Albuminuria following phenolphthalein ingestion.—*W. R. Bloor*: The determination of fats in small amounts of blood.—*L. Baumann*: Creatin determination in muscle.—*A. C. Kolls* and *A. S. Loevenhart*: A respiration chamber for small animals.—*J. R. Murlin*: A respiration incubator for the study of metabolism in new-born and prematurely-born infants.—*N. R. Blatherwick*: The specific role of foods in relation to the composition of the urine.—*Rita K. Chesnut*: Creatinin- and creatin-free foods.—*S. Bookman*: Experimental hydrochloric-acid intoxication.—*P. H. Mitchell*: The effects of water-gas tar on oysters.—*P. A. Shaffer*: The effect of glucose on autolysis; A possible explanation of the protein-sparing action of carbohydrates.—*M. X. Sullivan*: The passage of organic substances from plant to medium.—*M. E. Pennington*, *J. S. Hepburn* and *E. L. Connolly*: Studies on chicken fat; (VI) The factors influencing the acidity of the crude fat.

PRESENTED BY TITLE. *E. B. Hart* and *E. V. McCollum*: The influence of restricted rations on growth.—*E. B. Hart* and *E. V. Nelson*: Production of ammonia by herbivora as a protection against acidosis.—*E. B. Hart*, *E. V. McCollum* and *H. Steenbock*: The influence of restricted rations on reproduction.—*J. Rosenbloom*: Further studies on the quantitative chemical composition of urinary calculi.—*J. Rosenbloom*: On the quantitative chemical composition of gall stones.—*J. Rosenbloom* and *T. Diller*: Metabolism studies in a case of family periodic paralysis.—*F. T. Stewart*, *O. Bergeim* and *P. B. Hawk*: Calcium metabolism in thyro-parathyroidectomy.—*P. E. Howe* and *P. B. Hawk*: Variations in the hydrogen ion concentration of the urine of man accompanying fasting and the low- and high-protein regeneration periods.

**Executive proceedings.** ORGANIZATION OF THE FEDERATION. The Society voted its formal approval of the establishment of the Federation of American Societies for Experimental Biology, comprising the American Physiological Society, American Society of Biological Chemists and the American Society for Pharmacology and Experimental Therapeutics. The Society also voted in favor of admitting to the Federation the newly organized American Society for Experimental Pathology.

NEW MEMBERS: *F. C. Cook*, Bur. of Chem., U. S. Dep't of Agric.; *W. H. Eddy*, Columbia Univ.; *K. G. Falk*, Harriman Research Lab., N. Y. City; *A. D. Hirschfelder*, Univ. of Minn.; *E. C. Kendall*, St. Luke's Hosp., N. Y. City; *H. B. Lewis*, Univ. of Penn.; *R. S. Lillie*, Clark Univ.; *E. K. Marshall, Jr.*, Johns Hopkins Med. Sch.; *G. W. Raiziss*, Polyclinic Hosp., Phila.; *R. F. Ruttan*, McGill Univ.; *Shiro Tashiro*, Univ. of Chicago; *C. J. West*, Rockefeller Inst.

OFFICERS-ELECT: President—*Graham Lusk*; Vice-President—*C. L. Alsberg*; Secretary—*P. A. Shaffer*; Treasurer—*D. D. Van Slyke*; Additional members of the Council—*J. J. Abel*, *A. B. Macallum*, *T. B. Osborne*; Nominating Committee—*S. R. Benedict*, *H. S. Bradley*, *Otto Folin*, *W. J. Gies*, *J. H. Kastle*, *J. B. Leathes*, *P. A. Levene*, *L. B. Mendel*, *H. G. Wells*.

VOTE OF THANKS. A unanimous vote of thanks was extended by the Society to the individual members of the "Local Committee,"

to the University of Pennsylvania and to the Jefferson Medical College for the hospitality which the Society enjoyed.

ATTENDANCE. The following members were present at one or more of the sessions: J. J. Abel, C. L. Alsberg, S. Amberg, L. Baumann, S. P. Beebe, W. N. Berg, W. R. Bloor, H. C. Bradley, H. H. Bunzel, R. Burton-Opitz, E. D. Clark, F. C. Cook, H. D. Dakin, W. Denis, W. H. Eddy, Otto Folin, W. J. Gies, I. Greenwald, S. Hatai, R. A. Hatcher, P. B. Hawk, L. J. Henderson, P. E. Howe, W. H. Howell, R. Hunt, A. Hunter, N. W. Janney, W. Jones, I. S. Kleiner, P. A. Kober, J. B. Leathes, J. Loeb, A. S. Loevenhart, Graham Lusk, A. B. Macallum, J. J. R. Macleod, W. deB. MacNider, W. McK. Marriott, E. K. Marshall, Jr., J. Marshall, E. V. McCollum, F. H. McCrudden, H. McGuigan, L. B. Mendel, P. H. Mitchell, J. R. Murlin, V. C. Myers, T. B. Osborne, A. W. Peters, M. E. Pennington, G. W. Raiziss, A. N. Richards, A. I. Ringer, E. W. Rockwood, L. G. Rowntree, W. Salant, F. H. Scott, P. A. Shaffer, T. Sollmann, S. Tashiro, A. E. Taylor, F. P. Underhill, D. D. Van Slyke, C. Voegtlin, G. B. Wallace, H. G. Wells, R. T. Woodyatt.

V. THE AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS: FIFTH ANNUAL MEETING

John Auer, Secretary

The fifth annual meeting of the Pharmacological Society was held in Philadelphia on Monday and Tuesday, December 29 and 30, at Jefferson Medical College and the University of Pennsylvania. The scientific meetings were auspiciously inaugurated by a joint session of societies which form the Federation of American Societies for Experimental Biology. At the subsequent meetings of the Pharmacological Society the following papers were read and discussed:

**Scientific program.** FIRST SESSION. JEFFERSON MEDICAL COLLEGE, MONDAY, DECEMBER 29, 2.00 P. M. *G. B. Wallace* and *H. B. Meyers*: Uranium glycosuria.—*W. deB. MacNider*: A comparative study of the vascular response of the kidneys in animals nephritic from uranium nitrate.—*W. Salant* and *M. Kahn*: The production of glycosuria by zinc salts.—*W. Salant* and *M. Kahn*: Further observations on caffein glycosuria.—*C. L. Alsberg* and *C. S. Smith*:

Studies upon the long-continued feeding of saponin.—*J. Auer* and *S. J. Meltzer*: The effect of the inhalation of ether upon the irritability of the voluntary peripheral motor mechanism.—*T. S. Githens* and *S. J. Meltzer*: The irritability of muscle and motor nerve in chloroform anesthesia.—*T. S. Githens* and *S. J. Meltzer*: The cessation of respiration in deep ether anesthesia and its possible relation to the action of ether upon the peripheral motor mechanism.—*W. M. Boothby*: The anesthetic tensions of ether vapor for man.—*R. A. Hatcher* and *C. Eggleston*: Studies in the absorption of drugs.—*J. Auer* and *S. J. Meltzer*: Fatal action of magnesium sulphate by absorption from the intestines.—*P. Hanzlik*: Liberation of formaldehyde from hexamethylenamine in pathological fluids.

SECOND SESSION. UNIVERSITY OF PENNSYLVANIA, TUESDAY, DECEMBER 30, 9.00 A. M. *A. E. Cohn* and *F. R. Fraser*: On certain effects of digitalis administration on the human heart.—*J. D. Pilcher*: Quantitative studies of vagus stimulation and atropin.—*O. H. Plant*: Experiments on the cardiac action of camphor.—*I. D. Macht*: The action of sodium and potassium iodide on the heart and blood vessels.—*W. Salant* and *C. S. Smith*: The influence of sodium tartrate on the circulation.—*A. S. Loevenhart*: The pharmacological action of tetra-methyl ammonium chloride on the circulation and respiration.—*H. G. Barbour*: Two types of periodic respiration produced by morphin.—*D. E. Jackson*: The pharmacological action of certain substances on the lungs and respiration.—*P. A. Lewis* and *R. B. Krauss*: Some further observations on trypan-red iodine compounds.—*L. Taylor*: Clinical studies with caffein.—*W. Salant* and *S. Hecht*: Further observations on the action of ergot.—*W. Salant* and *C. S. Smith*: The toxicity of tin.

**Executive proceedings.** See page 280.

NEW MEMBERS: *A. E. Cohn*, Rockefeller Inst.; *H. F. Helmholtz*, Sprague Memorial Inst., Chicago; *W. A. Jacobs*, Rockefeller Inst.; *Hugh McGuigan*, Northwestern Med. Sch.

OFFICERS-ELECT: President—*Torald Sollman*; Secretary—*John Auer*; Treasurer—*W. deB. MacNider*; Additional members of the Council—*J. J. Abel*, *A. S. Loevenhart*; Membership Committee—*Reid Hunt* (term expires 1916).

DINNERS AND SMOKERS. Excellent subscription dinners of very moderate cost were an enjoyable feature of the meeting and were



attended not only by the members of the Federation but also by the naturalists and zoologists. They were held on the evenings of December 29 and 30 at the Walton Hotel and Kugler's Restaurant, respectively. There were only a few speeches. At the first dinner, Drs. W. W. Keen and S. J. Meltzer spoke; at the second dinner the naturalists presided and Dr. Raymond Pearl delivered a short address.

**VOTE OF THANKS.** At the last executive session of the Society a motion was passed unanimously to thank the local committee representing the University of Pennsylvania and Jefferson Medical College for the comprehensive and efficient way in which all arrangements for the meetings and the visitors' comfort were made. No names are mentioned in this expression of appreciation because the secretary is informed that practically every Philadelphia member of the four constituent societies labored on the local committee to make the first meeting of the Federation as enjoyable as possible.

#### VI. THE AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY: ORGANIZATION AND FIRST ANNUAL MEETING

G. H. Whipple, Secretary

**Executive proceedings.** **ORGANIZATION.** The American Society for Experimental Pathology was organized in a tentative way after the December meetings in Cleveland, in 1912. The general plan, constitution and membership list were completed informally during the time between that meeting and the one in Philadelphia. The formal organization of the Society was effected during the recent meeting in Philadelphia.

*Charter members:* J. F. Anderson, C. H. Bunting, Alexis Carrel, H. A. Christian, R. I. Cole, Harvey Cushing, C. W. Duval, D. L. Edsall, Simon Flexner, F. P. Gay, W. S. Halsted, Ludvig Hektoen, A. W. Hewlett, J. W. Jobling, H. T. Karsner, P. A. Lewis, Leo Loeb, W. T. Longcope, W. G. MacCallum, W. H. Manwaring, David Marine, S. J. Meltzer, H. Noguchi, F. G. Novy, E. L. Opie, W. H. Park, R. M. Pearce, M. J. Rosenau, E. C. Rosenow, Peyton Rous, Theobald Smith, G. N. Stewart, H. G. Wells, G. H. Whipple, Hans Zinsser.



*Constitution.* The following extracts from the constitution outline the purposes and policies of the society.

The object of the Society is to bring the productive investigators in pathology, working essentially by experimental methods, into closer affiliation with workers in other fields of experimental medicine. Any American investigator who, through the use of experimental methods, has, within three years prior to his candidacy, done meritorious work in pathology, is eligible to membership.

There shall be three classes of members: Active, emeritus and honorary members. *The number of active members shall not exceed forty.* Any active member of the Society may, after a lapse of five years, upon his or her request and the approval of the Council, be made an emeritus member. Honorary members may be elected from the active or emeritus list, or from the group of distinguished investigators at home or abroad, who have contributed to the knowledge of pathology by experimental study. They shall be elected only by the *unanimous* vote of the members present at the time of nomination.

Papers shall be limited, in time of oral presentation, to ten minutes. The Council may make provisions for the presentation of longer papers, the number of which shall not exceed two. The number of papers for each annual meeting shall not exceed twenty-five. The subjects of papers must be confined to experimental work in pathology. In doubtful cases a liberal interpretation by the President and Secretary may prevail. The Council may invite, however, presentations dealing with any subject which it considers of considerable interest to the Society.

OFFICERS-ELECT: President—*R. M. Pearce*; Vice-President—*J. F. Anderson*; Secretary-treasurer—*G. H. Whipple*; Additional members of the Council—*Harvey Cushing* and *David Marine* (succeeding *S. J. Meltzer* who, according to the provisional constitution, was elected for only one year).

NEW MEMBERS: No new active members were elected at the meeting. *William H. Welch* was elected an honorary member.

ATTENDANCE. The attendance at each meeting varied between 35 and 60. Twenty-two of the total membership of 35 attended the meetings.

ADMISSION TO THE FEDERATION. At the business meeting of the Federation of American Societies for Experimental Biology this Society was unanimously admitted to membership in the Federation.

Scientific program. FIRST SESSION. JEFFERSON MEDICAL COLLEGE, MONDAY, DECEMBER 29, 2 P. M. *W. Hale* and *J. F. Anderson*: An experimental demonstration of the cause of the unto-ward symptoms after intraspinal injections of serum.—*W. A. Dandy*: Hydrocephalus; An experimental study.—*H. Cushing* and *L. H. Weed*: The double source of the cerebrospinal fluid.—*P. Rous* and *J. B. Murphy*: The resistance to transplantable chicken tumors.—*P. Rous* and *L. Lange*: Certain spontaneous tumors as different manifestations of a single disease entity.—*L. Loeb*, *M. S. Fleisher* and *M. Vera*: Immunization against substances inhibiting tumor growth.

SECOND SESSION. UNIVERSITY OF PENNSYLVANIA, TUESDAY, DECEMBER 30, 2 P. M. *Martha Wollstein* and *S. J. Meltzer*: Pulmonary lesions produced by the *B. pyocyaneus*.—*M. C. Winternitz* and *B. S. Kline*: Experimental pneumonia; Studies by means of vital stains.—*M. J. Rosenau*: Some further experiments on poliomyelitis.—*Paul A. Lewis* and *A. G. Margot*: Some further observations on the relation of the spleen to the resistance of mice to experimental tuberculosis.—*J. W. Jobling* and *W. Petersen*: Substances influencing the production of caseation in tuberculosis.—*J. W. Jobling* and *W. Petersen*: Some enzyme-inhibiting substances.—*W. H. Park*: Immunity produced by toxin-antitoxin mixtures in man and animals.—*H. Zinsser* and *E. Carey*: The relation of normal opsonin to complement, as determined by methods of complement splitting.—*G. G. Lake* and *H. G. Wells*: The immunological reactions of the placenta proteins.—*E. W. Goodpasture*: Studies on fibrinogen.

THIRD SESSION. UNIVERSITY OF PENNSYLVANIA, WEDNESDAY, DECEMBER 31, 9 A. M. *H. A. Christian*: Some effects of diuretics in experimental nephritis.—*H. T. Karsner*, *O. Folin* and *W. D. Denis*: Studies of nitrogen retention in experimental acute nephritis.—*G. H. Whipple*: Intestinal obstruction; Studies in immunity reaction and protection against the toxic agent.—*J. H. King*: Experimental study of the pathology of the spleen.—*D. Marine*: Further

observations on goitre in fish; Its cure and prevention.—*W. H. Halsted*: The influence upon the thymus of bilobar excision of the thyroid gland.—*S. J. Crowe*: The effects of the successive reduction of the suprarenal glands of dogs.

*Laboratory of Biological Chemistry of Columbia University,  
College of Physicians and Surgeons, New York*

PROCEEDINGS OF SOCIETIES MEETING IN CON-  
JUNCTION WITH THE FEDERATION OF AMERI-  
CAN SOCIETIES FOR EXPERIMENTAL BI-  
OLOGY; AND OF THE SOCIETY OF  
AMERICAN BACTERIOLOGISTS

PAUL E. HOWE

PREPARED FROM REPORTS BY THE SECRETARIES,  
CASWELL GRAVE, BRADLEY M. DAVIS, CHARLES R. STOCKARD  
AND A. P. HITCHENS

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I. THE AMERICAN SOCIETY OF ZOOLOGISTS

Caswell Grave, Secretary

The Central and Eastern branches of The American Society of Zoologists met in joint session at the University of Pennsylvania, Philadelphia, December 29th, 1913, to January 1st, 1914, inclusive, in conjunction with The American Society of Naturalists, The American Association of Anatomists, and the Federation of American Societies for Experimental Biology. The *titles of papers* of particular biochemical interest are appended:

*J. F. McClendon*: On the parallelism between increase in permeability and abnormal development of fish eggs.—*A. Richards*: The effect of X-rays on the rate of cell division in the early cleavage of *Planorbis*.—*S. Morgulis*, *P. E. Howe* and *P. B. Hawk*: A microscopical investigation of tissues from dogs which fasted for extremely long periods of time.—*G. L. Kite*: The molar structure of protoplasm.—*Henry Laurens*: The reactions of normal and eyeless amphibian larvae to light.—*O. C. Glaser*: An analysis of the egg extractives of *Arbacia* and *Asterias*.—*A. A. Schaeffer*: Feeding

habits of *Ameba*.—*S. O. Mast*: Changes in pattern and color in fishes, with special reference to flounders.—*D. Hooker*: The reactions to light and darkness of the melanophores of frog tadpoles.—*G. G. Scott*: The oxygen utilization of fishes.—*A. A. Schaeffer*: Reactions of *Ameba* to light.—*H. S. Burr*: The feeding reactions of *Amblystoma* larvae.—*E. J. Lund*: Experimental analysis of certain processes in the food vacuole of *Bursaria*.—*W. C. Allee*: The relation between rheotaxis and resistance to potassium cyanide in *Isopoda*.—*V. E. Shelford*: The experimental modifications of tiger-beetle color-patterns by variation of temperature and moisture during ontogeny.—*L. J. Cole* and *C. L. Davis*: The effect of alcohol on the male germ cells, studied by means of double matings.

**Executive proceedings.** NEW CONSTITUTION. The Committee on Organization and Policy, appointed at the meeting held at Princeton, in 1911, submitted its report in the form of a new constitution, which, with certain amendments, was unanimously adopted.

PREMEDICAL EDUCATION. A committee consisting of Henry B. Ward, chairman, G. H. Parker and C. E. McClung, was appointed to confer with a committee of three from the American Association of Anatomists on the subject of *premedical education*.

"MATHEWS PLAN." The Mathews plan for the organization of an American Biological Society<sup>1</sup> was referred to the Executive Committee for consideration and report to a future meeting.

NEW MEMBERS: *Central Branch*—J. E. Ackert, R. Chambers, J. M. Elrod, E. H. Harper, F. Isely, Ruth Marshall, H. L. Wieman. *Eastern Branch*—G. C. Bassett, R. Binford, Maynie R. Curtis, H. D. Goodale, B. H. Grave, Emily R. Gregory, Louise H. Gregory, G. L. Kite, C. C. Little, E. C. McDowell, N. E. McIndoo, Edith M. Patch, Alice Robertson.

OFFICERS-ELECT: President—*C. E. McClung*; Vice-President—*M. F. Guyer*; Secretary-treasurer—*Caswell Grave*; Additional members of the Executive Committee—*H. E. Jordan*, *George Lefevre*, *H. F. Nachtrieb*, *A. F. Shull*, *H. V. Wilson*.

<sup>1</sup> BIOCHEMICAL BULLETIN, 1913, iii, p. 142.



II. THE AMERICAN SOCIETY OF NATURALISTS:  
THIRTY-FIRST ANNUAL MEETING

Bradley M. Davis, Secretary

The thirty-first annual meeting of the American Society of Naturalists was held in the Zoological Laboratory of the University of Pennsylvania on December 31, 1913. In affiliation with the Society this year were the American Society of Zoologists, the American Association of Anatomists, and the Federation of American Societies for Experimental Biology. The *titles of papers* of particular biochemical interest follow:

*L. J. Henderson*: The functions of an environment.—*Jacques Loeb*: On the adaptation of *Fundulus* to abnormal salt solutions.—*D. T. MacDougal*: Divergent characters of the progeny arising from seed maturing in treated ovaries of *Scrophularia occidentalis*.

The session of the afternoon consisted of a symposium on the subject: "The scope of biological teaching in relation to new fields of discovery." Papers were presented by M. F. Guyer, zoology; M. A. Chrysler, botany; R. R. Bensley, anatomy and medicine; G. H. Parker, general physiology.

The Naturalists' dinner was held on the evening of December 31, at the Hotel Walton, with one hundred and ten in attendance. The president's address by Prof. Ross G. Harrison was entitled "Science and practice."

**Executive proceedings.** CONSTITUTION AND BY-LAWS. A revised constitution and by-laws were adopted with several important modifications of the old constitution. The former division of the Society into an Eastern Branch and a Central Branch was abolished. "Sections of the Society may be organized in any locality, with the approval of the Society in each case, by ten or more members, for the purposes of holding meetings for the presentation of scientific papers. Such sections shall have the right to elect their own officers and associate members, but associate membership in any section shall not confer membership in the Society."

NEW MEMBERS: *I. W. Bailey*, Harvard Univ.; *A. M. Banta*, Carnegie Station for Exp. Evol'n; *H. H. Bartlett*, Bur. of Plant Industry, U. S. Dep't of Agric.; *C. T. Brues*, Harvard Univ.; *P. P. Calvert*, Univ. of Penn.; *M. A. Chrysler*, Univ. of Me.; *R. A.*

*Gortner*, Carnegie Station for Exp. Evol'n; *M. J. Greenman*, Wistar Inst.; *R. W. Hegner*, Univ. of Mich.; *L. J. Henderson*, Harvard Univ.; *M. H. Jacobs*, Univ. of Penn.; *G. L. Kite*, Henry Phipps Inst'n; *R. S. Lillie*, Clark Univ.; *C. E. McClung*, Univ. of Penn.; *J. H. McGregor*, Columbia Univ.; *E. B. Meigs*, Wistar Inst.; *J. P. Moore*, Univ. of Penn.; *Alice Robertson*, Wellesley Coll.; *E. W. Sinnott*, Harvard Univ.; *A. B. Stout*, N. Y. Botan. Garden; *P. W. Whiting*, Harvard Univ.

OFFICERS-ELECT: President—*S. F. Clarke*; Vice-President—*F. R. Lillie*; Secretary—*B. M. Davis*; Treasurer—*J. A. Harris*; Additional members of the Executive Committee—*R. G. Harrison*, *E. P. Lyon*, *Raymond Pearl*.

### III. THE AMERICAN ASSOCIATION OF ANATOMISTS: THIRTIETH ANNUAL MEETING

Charles R. Stockard, Secretary

The thirtieth annual meeting of the American Association of Anatomists was held at the University of Pennsylvania, in Philadelphia, on December 29–31, 1913, in conjunction with the Zoologists and Naturalists, and the Federation of American Societies for Experimental Biology. The *papers* of particular interest to biological chemists are listed below:

*E. R. Clark*: On certain morphological and staining characteristics of the nuclei of lymphatic and blood-vascular endothelium and of mesenchyme cells in chick embryos.—*H. M. Evans*: The relation between chemical constitution, physical behavior, and ability of the benzidine dyes to act as vital stains.—*D. Hooker*: The development of pigment in a frog.—*R. H. Whitehead*: Vital staining of the interstitial cells of the testis.

DEMONSTRATIONS. *W. H. F. Addison*: The Frankfurt method of mounting microscopic sections in gelatin, without the use of a coverglass.—*H. H. Bullard*: Demonstration of fat in the muscle fibers of the myocardium and of the atrio-ventricular system.—*M. R. Chase*: Pyridine-silver preparations of the vagus nerve of man, dog and cat.—*E. V. Cowdry*: The staining of mitochondria in the human lymphocytes with janus green.—*H. M. Evans*: Preparations illustrating vital staining with various benzidine dyes.—*S. W. Ran-*

son: Pyridine-silver preparations of the spinal cord of the cat and the Rhesus monkey.—*Katherine J. Scott*: Preparations showing the vital stain applied to the study of wound healing.—*R. E. Sheldon*: Preparations and drawings showing the results of a modified Weigert technique, applied to serial paraffin sections of the adult brain.—*H. G. Weiskotten* and *H. S. Steensland*: On the nature of the fat cells.—*H. S. Steensland*: Marchi technique: Safer and easier clearing and mounting of sections.

**Executive proceedings.** NEW MEMBERS: *E. A. Baumgartner*, Univ. of Minn.; *H. Bayon*, Tulane Univ.; *T. H. Bryce*, Univ. of Glasgow; *F. P. Chillingworth*, Tulane Univ.; *Eleanor L. Clark*, Johns Hopkins Med. Sch.; *G. W. Corner*, Johns Hopkins Med. Sch.; *R. S. Cunningham*, Johns Hopkins Med. Sch.; *A. C. Geddes*, McGill Univ.; *S. R. Guild*, Univ. of Mich.; *G. V. A. Kappers*, Internat. Central Inst. for Brain Research, Holland; *H. S. Murphy*, Univ. of Ia.; *D. A. Rheinhart*, Indiana Univ.; *A. Robinson*, Univ. of Edinburgh; *Katherine J. Scott*, Johns Hopkins Med. Sch.; *P. G. Shipley*, Johns Hopkins Med. Sch.; *R. W. Shufeldt*, U. S. A. (Retired); *G. E. Smith*, Victoria Univ.; *P. G. Snow*, Univ. of Utah; *J. Symington*, Queens Univ.; *J. Thorkelson*, Coll. of Physicians and Surgeons, Balt.; *R. West*, Columbia Univ.; *J. T. Wilson*, Univ. of Sydney.

OFFICERS-ELECT: President—*G. C. Huber*; Vice-President—*F. T. Lewis*; Secretary-treasurer—*C. R. Stockard*; Additional members of the Executive Committee for the term expiring in 1917—*C. J. Herrick*, *W. H. Lewis*.

VOTE OF THANKS. On motion the Association tendered its sincere thanks and appreciation of Professor Piersol and the members of his staff and the local committee, and to Provost Smith and other officers of the University of Pennsylvania for the very efficient arrangements made and for their hearty cooperation in furthering the success of this meeting.

RESOLUTION ADOPTED: "That this Association accepts with regret the resignation of Dr. G. Carl Huber from the office of Secretary-Treasurer and desires to place on record its high appreciation of his services and its recognition of the prominent part he has taken in bringing the Association to its present prosperous condi-

tion, and in advancing the cause of anatomy on this continent both by precept and example."

#### IV. THE SOCIETY OF AMERICAN BACTERIOLOGISTS: FIFTEENTH ANNUAL MEETING

A. P. Hitchens, Secretary

The Society of American Bacteriologists met in Montreal, Canada, December 31, 1913 to January 2, 1914, in the new medical building of McGill University. President Winslow's address, on The characterization and classification of bacterial types, was delivered at the annual dinner held at the University Club (*Science*, 1914, xxxix, p. 77). A list of the *papers* of particular interest to the biochemist follows:

*P. E. Brown*: Bacterial activities and crop production.—*C. B. Lipman*: Antagonism between salts as affecting soil bacteria.—*P. E. Brown* and *E. H. Kellogg*: Sulfofication in soils.—*T. D. Beckwith* and *A. F. Vass*: A possible improvement of the technique of determination of the ammonifying power of soils.—*Caroline Derick*: On the influence of hypochlorite treatment of potable waters upon their diatomaceous content.—*C. H. Higgins*: Toxic products in foods and their detection.—*S. C. Prescott*: Bacteriological changes in certified milk at low temperatures.—*F. P. Gorham*: Report of the committee on methods of identification of bacterial species.—*Jean Broadhurst*: Constancy in fermentative reactions of streptococci.—*L. A. Rogers*, *W. M. Clark* and *Alice C. Evans*: The significant characters of the colon group isolated from cow feces.—*I. J. Kligler*: Studies on the classification of the colon group.—*J. A. Sperry*: A biochemical study of proteins with reference to the ability of bacteria to break down and utilize pure animal and vegetable proteins.—*W. L. Owen*: Bacteriology in relation to the cane sugar industry; its problems and possibilities.—*Lewis Davis*: A study of the tellurite reaction with the colon-typhoid group.—*F. M. Meader*: The precise technic for obtaining the Gruber-Widal reaction.—*S. H. Ayres*: A synthetic medium for the detection of the colon group.—*F. P. Gorham*, *J. C. Hebden* and *B. S. Levine*: The use of bacterial cultures in treating textile fibers.—*A. A. Bruere*: A method of preserving complement.—*J. L. Todd*: *Spirochacta recurrentis* and its immunity reactions.—*J. B. Brenner*: The value of the new

skin test in tuberculosis.—*F. Gurd*: On the relationship of allergic and opsonic reactions.—*L. F. Rettger*: A comparative study of the intestinal flora of animals provided with normal and experimental diets.

*Research.* An announcement was made at the meeting that the Division of Carbohydrate Investigations of the Bureau of Chemistry, U. S. Dep't of Agriculture, has perfected improved methods for preparing in a high state of purity several of the carbohydrates used for the identification and classification of many bacteria. The Bureau has arranged to supply small quantities of these carbohydrates to bacteriologists who are engaged in public-health work in connection with the enforcement of food laws. The Division also offers to collaborate with members of the Society who would like to obtain small quantities of these sugars for use in their biological work, particularly for use in research. This announcement was welcomed as one of great importance to bacteriologists generally.

*Biochemical Laboratory of Columbia University,  
College of Physicians and Surgeons, New York*



## THE BIOCHEMICAL SOCIETY, ENGLAND

R. H. A. PLIMMER, SECRETARY

At the meeting in the Physiological Laboratory, King's College, London, on Wednesday, November 12th, 1913, at 5.30 p. m., Prof. W. D. Halliburton, F.R.S., in the chair, the following communications were given:

*O. Rosenheim and J. C. Drummond*: The estimation of ethereal and inorganic sulphates in urine by a volumetric method.

*O. Rosenheim*: The constitution of the brain galactosides.

*Mrs. M. C. Rosenheim* (introduced by O. Rosenheim): The occurrence of spermine in pancreas and a note on the preparation of spermine phosphate from testis and other organs.

*J. A. Gardner and Mr. Lauder*: On the cholesterol content of the tissues of cats under various dietetic conditions.

*S. B. Schryver*: The clotting of caseinogen by pancreatin.

At the meeting at the Lister Institute, Chelsea Gardens, London, S. W., on Tuesday, December 9th, 1913, at 5.30 p. m., Prof. A. Harden, F.R.S., in the chair, the following communications were given:

*S. Walpole*: The mutual precipitation of similarly charged colloids.

*R. H. A. Plimmer and Miss R. F. Skelton*: The quantitative estimation of urea and indirectly of allantoin in urine by means of urease.

*H. H. Dale and A. J. Ewins*: A hitherto undescribed active principle of ergot.

*E. E. Atkin*: Demonstration of unpolarisable electrodes for use in cataphoresis experiments.

*H. Chick and E. Lubrynska*: The viscosity of protein solutions.

*H. Maclean*: The estimation of sugar in small quantities of blood.

*University College, London*

FOURTEENTH SCIENTIFIC MEETING OF THE CO-  
LUMBIA UNIVERSITY BIOCHEMICAL ASSOCIA-  
TION AT THE COLLEGE OF PHYSICIANS  
AND SURGEONS, NEW YORK,  
DECEMBER 5, 1913<sup>1</sup>

PROCEEDINGS REPORTED BY THE SECRETARY,

ALFRED P. LOTHROP

The *fourteenth scientific session* of the Columbia University Biochemical Association was held at the Columbia Medical School, at 4:15 P. M., on Dec. 5, 1913. Abstracts of the papers are presented here (pages 303-314) in two groups: (*A*) *Abstracts of papers on research by non-resident members*<sup>2</sup> and (*B*) *abstracts of papers from the Columbia Biochemical Department and affiliated laboratories*. The appended summary facilitates reference to the abstracts (108-119).<sup>3</sup>

A SUMMARY OF THE NAMES OF THE AUTHORS AND OF THE  
TITLES OF THE SUCCEEDING ABSTRACTS (108-119)

A

- |   |   |
|---|---|
| S. GITLOW and B. HOROWITZ. A rapid clinical test for hyperglycemia. (108)                             | MAX KAHN and CHARLES J. BRIM. Urinary catalase in health and disease. (112) |
| B. HOROWITZ. The action of ammonia on phenols. (109)  | I. J. KLIGLER. Studies on the classification of the colon group. (113)      |
| MAX KAHN. A clinical method for the quantitative estimation of sugar in small amounts of blood. (110) | MATTHEW STEEL. A study of the influence of electricity on metabolism. (114) |
| MAX KAHN. Clinical studies of the Russo test. (111)   |   |

<sup>1</sup> Scientific meetings are held *regularly* on the first Fridays of December, February and April, and on the first Monday in June. Proceedings of the thirteenth and fifteenth scientific meetings are published at pages 331 and 334.

<sup>2</sup> Members of the Association who were not *officially* connected with the Columbia Biochemical Department when the researches were conducted.

<sup>3</sup> Previous abstracts were published in the *BIOCHEMICAL BULLETIN*: 1-44, 1912, ii, p. 156; 45-62, 1913, ii, p. 285; 63-72, 1913, ii, p. 452; 73-85, 1913, ii, p. 462; 86-107, 1913, ii, p. 541.

## B

- WILLIAM J. GIES. Exhibition of a large mass of mixed lipins that had been dialyzed through rubber. (115)
- MAX KAHN and WILLIAM J. GIES. A further study of the biochemical origin of sulfocyanate. (116)
- CHARLES C. LIEB and WILLIAM J. GIES. A further study of the pharmacology of sulfocyanate. (117)
- ALFRED P. LOTHROP and WILLIAM J. GIES. A further study of dental caries. (118)
- ARTHUR W. THOMAS. The organic constituents of raw and burned soils. (119)

A. ABSTRACTS OF PAPERS ON RESEARCH BY NON-RESIDENT MEMBERS<sup>4</sup>

108. A rapid clinical test for hyperglycemia. S. GITLOW AND B. HOROWITZ. (*Biochemical Laboratory, Fordham University Medical School.*) Published in full in this issue of the BIOCHEMICAL BULLETIN at page 272.

109. The action of ammonia on phenols. B. HOROWITZ. (*Biochemical Laboratory, Fordham University Medical School.*) This work was a continuation of that done on the action of ammonia on thymol.<sup>5</sup> The phenols selected were the following: Phenol, *m*-cresol, thymol,  $\alpha$ -naphthol, tyrosin, resorcin, orcin, vanillin, phloroglucinol and pyrogallol. To 0.5 gm. of substance, 100 c.c. of 10 percent ammonium hydroxide sol. were added and the solutions allowed to stand. All developed colors sooner or later; tyrosin, very slowly. These colorations were different with each phenol, but none even remotely approached the beautiful blue that thymol yielded. Extraction of the alkaline liquids with ether gave colorless layers for all except naphthol (light dirty brown), and thymol (beautiful red or reddish violet). *This, then, is a distinguishing test for thymol.* Equal quantities of the colored products were mixed and extracted with ether. The ether layer at first showed the pink (thymol) color, but later assumed a brownish tinge.

It has been shown in the case of thymol that oxygen is an important factor in the color formation. The amount of oxygen absorbed was measured by inverting a thymol-ammonia mixture over water, and measuring the rise of the liquid in the tube. Analogous

<sup>4</sup> Members of the Association who were not *officially* connected with the Columbia Biochemical Department when the researches were conducted.

<sup>5</sup> Gies: BIOCHEMICAL BULLETIN, 1912, ii, p. 171; 1913, ii, p. 293. Horowitz: Dissertation; Columbia University, 1913. Pp. 68.

procedures were employed with the phenols under consideration. All, except tyrosin, showed oxygen absorption or rather, combination with oxygen. Curves having the time element for abscissae and heights of liquid in tube for ordinates, brought out the interesting fact that *the rate of oxygen absorption, or the rate of intensity of color formation, bears a direct relationship to the number of OH groups in the phenol.* The work is now being continued along the following lines: The application of the foregoing methods to all obtainable compounds containing the phenolic grouping; the colorimetric measurement of the *rate* of color formation; the spectroscopic behavior of the different colored products; and the isolation and examination of the pigments.

This research, which is being carried out under Professor Gies' direction, may have an important bearing on plant pigments; and it is in connection with work on the latter, in which Professor Gies and the author are engaged, that it has been undertaken.

110. A clinical method for the quantitative estimation of sugar in small amounts of blood. MAX KAHN. (*Washington, D. C.*) The test recommended is based on Bang's<sup>6</sup> process. Control tests were made with various known solutions of glucose and accurate quantitative results were obtained. The process is very simple and should require not more than ten to fifteen minutes for the whole analysis.

Two solutions are prepared in the following manner: (a). *Copper solution.* Dissolve 500 gm. of potassium carbonate, 400 gm. of potassium sulfocyanate and 100 gm. of potassium bicarbonate in 1200 c.c. of water, warming if necessary to 50–60° C., and then cooling to room temperature. Add 150 c.c. of an aqueous solution of 25 gm. of copper sulfate (crystallized). The sol. is then made up to 2000 c.c.; it keeps indefinitely. (b). *Hydroxylamine solution.* Dissolve 200 gm. of potassium sulfocyanate in 1500 c.c. of water and add a sol. of 6.55 gm. of hydroxylamine sulfate in water. Make up with water to 2000 c.c. This sol. also keeps well in a dark colored bottle. Equal volumes of these two solutions should exactly correspond to each other. The presence of proteins does *not* interfere with this test.

<sup>6</sup> Bang: *Zeit. f. physiol. Chem.*, 1909, lxiii, p. 443; *ibid.*, 1910, lxv, p. 497; *Biochem. Zeit.*, 1908, vii, p. 327; *ibid.*, 1909, xi, p. 538; *Hammarsten-Festschrift*, 1906, No. 2.

Into a weighing flask put 15 c.c. of the copper sol. from a graduated buret, and weigh the flask together with the liquid. An ear lobe of the patient is pricked and 15 drops of blood are allowed to fall directly into the copper sol. in the weighing flask. In experimenting with rabbits it is quite easy to insert a needle of large caliber into an ear vein and thus draw off 15–20 drops of blood, the needle acting like a canula. The flask is now weighed a second time, and the amount of blood taken for analysis is thus determined.

The blood and the copper sol. in the flask are brought to a boil and filtered through a Gooch filter with suction. The coagulum is washed until the washings are perfectly colorless, 10–15 c.c. of water being sufficient for such washing. The washings are united with the filtrate and titrated with the hydroxylamine sol., which is added slowly from a graduated buret until all trace of blue or green disappears from the filtrate. Since 1 c.c. of the hydroxylamine sol. exactly decolorizes 1 c.c. of the copper sol., the amount of copper present in excess is thus determined, and the difference between the original amount of copper and the excess represents the copper reduced by the sugar in the blood.

With this method a number of determinations of sugar in the blood were carried out. In most instances the results obtained by the above process were higher than the figures given by previous observers, presumably due to more accurate manipulation because of the greater simplicity of the method.

It was found that normal human blood contained from 0.14–0.19 percent of sugar. The blood of a diabetic patient who had a glycosuria of 2.7 percent contained 0.37 percent. Two nephritic patients had 0.21 percent (chronic interstitial nephritis) and 0.11 percent (acute parenchymatous nephritis) of sugar in the blood. In a very large number of analyses of the blood of rabbits, it was found that the normal sugar content varied between 0.11 and 0.18 percent. Feeding sugar to rabbits raised the sugar content of the blood to 0.24 percent. Subcutaneous administration of caffeine (150 mg. per kilo of body weight) induced marked hyperglycemia, the highest figure observed being 0.385 percent. While zinc causes a marked glycosuria (by intravenous administration of the malate), it does not produce hyperglycemia; the sugar content of the blood in these cases seems to be normal or subnormal.



A comparison of the several methods recently recommended for the determination of sugar in small quantities of blood was undertaken. The methods studied were those of Bang,<sup>7</sup> Forsbach and Severin,<sup>8</sup> and Kowarski.<sup>9</sup> The method of Bang is a clinical one, and is not intended for quantitative purposes. I have had no success with it whatever, and this test seems to be of rather doubtful value. The method is conducted as follows: A few drops of blood are taken on a small piece of filter paper; the paper is put into a test tube and treated with 5 c.c. of a boiling sol. of potassium chloride. After cooling, a few drops of Fehling sol. are added and the mixture is boiled for half a minute. If no reduction is observed, the sugar is below 0.15 percent.

The two other methods are very complicated. The one of Forsbach and Severin is colorimetric, and that of Kowarski is titrimetric.

**III. Clinical studies of the Russo test.** MAX KAHN. (*Beth Israel Hospital Chemical Laboratory.*) The Russo test is carried out as follows: To 5 c.c. of filtered, freshly voided urine add two or three drops of a 1 percent aqueous sol. of methylene blue. An emerald green color signifies a positive result; the slightest trace of blue is to be taken as a negative result. Russo recommended this test as a method for diagnosing typhoid fever. In a series of tests carried out on 269 patients for a period of several days, it was found that positive results were obtained not only in typhoid cases but also in advanced tuberculosis, malaria, typhus, septic infections, biliary disease, advanced carcinoma and cerebro-spinal meningitis. Children suffering from empyema invariably reacted positively to this test. In all of the urines the Ehrlich diazo test was also applied. It was found that in typhoid fever the Russo test is positive several days before the diazo reaction, and lasts a few days after the diazo reaction disappears. Except in cases of advanced tuberculosis and advanced carcinomatosis, the diazo reaction was negative when the Russo test was positive. In infants and young children suffering from cardio-nephritis it was often found that both the diazo and the Russo tests were positive.

<sup>7</sup> Bang: *Münchener med. Wochenschr.*, 1913, lx, p. 2277.

<sup>8</sup> Forsbach and Severin: *Archiv f. exp. Path. u. Pharm.*, 1912, lxviii, p. 341.

<sup>9</sup> Kowarski: *Deutsche med. Wochenschr.*, 1913, xxxix, p. 1635.

112. **Urinary catalase in health and disease.** MAX KAHN AND CHARLES J. BRIM. (*Beth Israel Hospital Chemical Laboratory.*) Traces of catalase were found in normal urine that had been freshly voided. In the urines of 75 patients suffering with various ailments, the catalase content varied. It was found especially high in urines that reacted positively for blood, bile or acetone. Quite a number of urines of patients suffering from cancer were tested for catalase, and no variation from the normal was observed, except in those cases where the liver was involved and the urine contained biliary pigments, or where the disease was very advanced and the urine showed the presence of acetone. Four cases of lymphosarcoma and Hodgkin's disease gave very high catalase content in the urine. In severe diabetes, patients with acidosis eliminated very largely increased amounts of catalase in the urine; on the other hand, diabetics who had no acetonuria showed no variation in the amount of urinary catalase. Typhoid fever patients and others with general septic infections excreted considerable catalase in the urine.

113. **Studies on the classification of the colon group.** I. J. KLIGLER. (*Department of Public Health, American Museum of Natural History.*) Eighty organisms, generally classed under the colon group, were subjected to a series of fermentative and other tests with a view of determining their natural grouping as based on biometric principles. The following tests were employed: (1) Morphology, gram; (2) fermentation of glucose, lactose, sucrose, raffinose, glycerol, mannite, dulcitol, salicin and inulin; (3) coagulation of milk; (4) liquefaction of gelatin; (5) production of indol; (6) reduction of nitrate; (7) V and P reaction. Fifty-seven of the strains fell into the lactose-fermenting division; twenty did not ferment lactose, but fermented glucose; three failed to ferment sugars.

Acid production, as determined by titrating aliquot portions of the broth with phenolphthalein as an indicator, was found to be a more constant and a more reliable differential test than gas production, as ordinarily determined. The degree of initial acidity had no appreciable effect on the final acidity, which was quite constant, reaching its maximum on about the fourth day.

The fifty-seven lactose-fermenters attacked mannite, glycerol,

sucrose, salicin, raffinose, dulcitol and inulin, in the order named. Mannitol, raffinose and inulin were found to be of minor or doubtful importance as a basis for classification. Sucrose divides the lactose group into two distinct sub-groups.

On subdividing the sucrose groups on the basis of dulcitol- and salicin-fermentation, respectively, it was found that the sucrose-salicin groups gave better correlation with indol production, V and P reaction, and gelatin liquefaction, than did the sucrose-dulcitol groups.

The sucrose-positive, salicin-positive group corresponds to *B. aerogenes*.

The sucrose-positive, salicin-negative group corresponds to *B. communior*.

The sucrose-negative, salicin-positive group corresponds to *B. communis*.

The sucrose-negative, salicin-negative group corresponds to *B. acidi-lactici*.

Glycerol was found to be of value in separating the cloacae forms from the aerogenes bacilli, 78 percent of the sucrose-positive, salicin-positive, glycerol-negative strains being liquefiers.

It must be borne in mind, of course, that this classification was obtained with a relatively small number of organisms and can at best be considered only tentative. The results are, however, sufficiently interesting to merit further investigation, especially on the part of those interested in the bacteriology of water.

Of the glucose-positive, lactose-negative forms, five liquefied gelatin and fermented glucose and sucrose, but failed to ferment any of the other substances, with the exception of glycerol, which was fermented by two of the organisms. Of the other tests, all were negative with the exception of indol, which was negative for the two glycerol-positive organisms and positive for the glycerol-negative. For the present all the five may be grouped under the name *B. vulgaris*.

The sixty-two members of the colon group discussed may, therefore, be said to fall into six main species as follows:

Species	Specific Tests	No. of Organisms
<i>B. communior</i> .....	gluc.+, lac.+, suc.+, sal.—	12
<i>B. communis</i> .....	gluc.+, lac.+, suc.—, sal.+	11
<i>B. aerogenes</i> .....	gluc.+, lac.+, suc.+, sal.+	19
<i>B. acidi-lactici</i> .....	gluc.+, lac.+, suc.—, sal.—	6
<i>B. cloacæ</i> .....	gluc.+, lac.+, suc.+, sal.+, glyc.—	9
<i>B. vulgaris</i> .....	gluc.+, lac.—, suc.+, gel.+	5

#### 114. A study of the influence of electricity on metabolism.<sup>10</sup>

MATTHEW STEEL. (*Long Island Medical College.*) In two experiments, eleven days each, a normal healthy adult on a uniform non-purin diet, was subjected for 30 minutes to Faradic sinusoidal currents of uniform strength (the secondary coil was over the primary 10 cm.) but of different frequencies of interruption, which were 45 per minute in experiment I, and 90 per minute in experiment II. The following symptoms were noted: A languid and tired feeling, strong desire to urinate, and increase in the daily volume of urine varying from 100 to 200 c.c. per day. There was a slight increase in the total nitrogen and creatinin nitrogen for the periods of treatment. The amounts of the other nitrogenous constituents were remarkably constant through all the periods.

During the course of determinations of urea by the Benedict method, urorosein developed in the specimens voided during the period of the electrical treatment. Herter has shown a relationship between the development of nitrites in urine and the appearance of urorosein. The specimens which gave the urorosein reaction, apparently as a result of the electrical treatment, responded strongly to tests for nitrites, whereas the normal specimens (which did not contain urorosein) were free from nitrites.

This study will be continued with other kinds of electrical currents.

#### B. ABSTRACTS OF PAPERS FROM THE COLUMBIA BIOCHEMICAL DEPARTMENT AND AFFILIATED LABORATORIES

115. Exhibition of a large mass of mixed lipins that had been dialyzed through rubber. WILLIAM J. GIES. The author exhibited 360 grams of mixed lipins that had been dialyzed, in five days, from 400 grams of butter. The latter had been dissolved in

<sup>10</sup> Steel: BIOCHEMICAL BULLETIN, 1913, ii, p. 547.



about 600 c.c. of ether, the solution divided into twelve equal parts and each twelfth portion, after transference to a rubber condom, supported in about 250 c.c. of ether in a glass-stoppered bottle. The dialysate was removed daily and fresh ether substituted. The volumes in the bags increased daily to the end. The ether in the mixed dialysates (a total of 8 liters) was eliminated by evaporation before an electric fan. The lipin residue (360 grams; 90 percent) looked like the original butter but was softer. The undiffused lipin mass from the ether in the bags (40 grams from 2500 c.c.) resembled the original butter but was harder. At the conclusion of the experiment the rubber bags were found, with the aid of indiffusible pigments, to be free from mechanical imperfections.

The massiveness of the main product indicated, in an impressive way, the ease, rapidity and completeness with which some lipins diffuse from ether through rubber into ether.

**116. A further study of the biochemical origin of sulfocyanate.**<sup>11</sup> MAX KAHN AND WILLIAM J. GIES. New experiments on dogs, involving determinations of the amounts of sulfocyanate in the blood, some of the tissues, gastro-intestinal contents, the urine and feces, after (a) administration of acetonitril, mandelic-acid nitril, amygdalin, glyocol, alanin and leucin; (b) after fasting and overfeeding with protein; (c) and after perfusion of blood, with and without acetonitril, through the liver, warrant the following general conclusions:

Sulfocyanate arises in the body from proteins and other substances that yield  $\text{—CN}$  and  $\text{—SH}$  radicals. Its quantity in any part of the body appears to depend primarily upon the available metabolic supply of  $\text{—CN}$  radicals.

The liver appears to be the chief site of sulfocyanate synthesis. The process of production in the liver seems to be essentially one of detoxification (defense) prior to excretion of sulfocyanate in bile and urine, as in the case of the conversion of indol into indican and the urinary elimination of the latter.

The radicals involved in the production of sulfocyanate are evidently of both exogenous and endogenous derivation under ordinary circumstances.

<sup>11</sup> Conducted under the auspices of the Dental Society of the State of New York. See *Dental Cosmos*, 1914, lvi, p. 175.



Salivary sulfocyanate appears to be wholly excretory in character and significance. After the administration of sulfocyanate it is promptly ejected through all the secretory channels including the salivary glands. Dog saliva, which is normally free from sulfocyanate, contains sulfocyanate in abundance after its systemic introduction.

117. **A further study of the pharmacology of sulfocyanate.**<sup>12</sup> CHARLES C. LIEB AND WILLIAM J. GIES.<sup>13</sup> Numerous experiments on animals and men yielded results which may be stated in general terms as follows:

*Therapeutic* doses of sodium sulfocyanate (in cats and dogs under anesthesia) were practically without effect on respiration, heart-rate, blood pressure, secretion of saliva, secretion of bile and excretion of urine.

Daily *therapeutic* doses of sodium sulfocyanate (in three men under observation for from two to three weeks at a time in each case) induced no unfavorable effects on heart-rate or blood pressure.

The sulfocyanates of sodium and potassium, in therapeutic proportions, exerted no appreciable systemic action. The observed toxicity of the potassium salt in such doses was due solely to the potassium ion.

We believe, in harmony with the results of our experiments, that there is nothing about the *known* qualities of sulfocyanate to indicate that sulfocyanate is able, *in the proportions of its normal occurrence in saliva*, to affect the secretory tendencies of the salivary or buccal glands, to modify the oral membranes, to influence the teeth from any standpoint, or to stimulate or retard or alter the activities of the oral micro-organisms. To attribute to sulfocyanate any such power is to do so empirically and without any present evidence in support of such an opinion.

The proportions of sulfocyanate that normally occur in the blood, lymph, tissues, secretions, and excretions appear to be wholly devoid of toxic or physiological effects.

<sup>12</sup> Conducted under the auspices of the Dental Society of the State of New York. See *Dental Cosmos*, 1914, lvi, p. 175.

<sup>13</sup> The pharmacological observations were made in the Pharmacological Laboratory, by Dr. Lieb, with the senior author one of the subjects.

118. A further study of dental caries.<sup>14</sup> ALFRED P. LOTHROP AND WILLIAM J. GIES. The effect of vinegar as a dentifrice was determined. Natural extracted teeth (16), nearly all of which contained typical fillings of gutta percha, silicate cement, oxy-phosphate of zinc, synthetic porcelain, red copper cement, alloy, amalgam, cast gold inlay and malleted gold,<sup>15</sup> were embedded in blocks of paraffin about three-fourths of an inch square, in such a way as to completely cover the roots with the paraffin, leaving only the enamel surfaces with the fillings exposed. These blocks, containing the teeth, were then placed in a narrow zinc box about 8 in. long and 1 in. deep, in such a way that the lower edges of the exposed surfaces were on a line with the edges of the box. The box was then completely filled with melted paraffin which, after hardening, made an "artificial jaw" in which the teeth were firmly fixed.

An ordinary flat toothbrush with tufted bristles was used for the application of dentifrices. At each application the brush was held a moment in running water, the bulk of the suspended water dislodged with a jerk, and then ten drops of diluted vinegar (1:1) or of a popular, slightly alkaline, antiseptic dentifrice were allowed to fall on the wet brush from a dropping bottle. The teeth were vigorously and systematically brushed for a period of 10 to 15 seconds. The brush was then rinsed in running water, and the teeth washed with the water that remained in the brush. The teeth were washed in this way with three fresh supplies of water. Finally, after residual water had been drained from the teeth by simply tilting the box, saliva was expectorated on the teeth and distributed over them with the clean brush. During the intervals between brushings (which occurred twice daily), each box of teeth was kept in a moist chamber, for which purpose the senior author's glass device for the preservation of hashed meat by the cold-storage

<sup>14</sup> Conducted under the auspices of the First District Dental Society of the State of New York. See the *Journal of the Allied Dental Societies*, 1913, viii, p. 283.

<sup>15</sup> The teeth were obtained for us and the fillings inserted by Drs. J. Morgan Howe and C. C. Linton. Before the experiment was begun, Drs. A. H. Merritt and C. C. Linton made critical examinations of the teeth with special reference to the detection by them, subsequently, of any unfavorable change as a result of our intended treatment of the teeth.

method was employed, with exceptional advantage.<sup>16</sup> A small amount of water was kept on the bottom of the chamber and the "artificial jaw" was supported at a level therein, on flat pieces of cork. By maintaining closure with the glass lid, the atmosphere in the chamber above the teeth was kept saturated with water, and the saliva on and around the teeth was prevented from evaporating. *The conditions for bacterial activity were especially favorable because of the stagnation of the fluid.*

The conditions of these experiments were such as to favor (a) the *maximum* destructive effect, if any, of the liquids used as dentifrices, and (b) the *minimum* protective influence of the saliva. The *normal* conditions in the mouth, it seems to us, would permit less destructive activity by the acid (if there was any such action), and would possess greater protective potential.

One set of seven teeth has been treated twice daily, since June 6, 1913 (six months), with vinegar (apple cider) diluted, half and half, with water; a second set of nine teeth has been simultaneously treated with a popular, slightly alkaline, antiseptic dentifrice.

These two sets of teeth were exhibited and examined at a meeting of the First District Dental Society of the State of New York, at the N. Y. Academy of Medicine, on Oct. 6, 1913. Drs. Merritt and Linton reported (then, orally; again, by letter on Dec. 2) that they were unable to detect any change, whatever, in these teeth as a result of the treatments, except that the filling of oxy-phosphate of zinc in one of the teeth, in the series treated with vinegar, was "very considerably washed out . . . due, probably, to the abrasive action of the brush and partly to the solvent action of acid in the vinegar" (Dr. Merritt).<sup>17</sup>

The proposed use of dilute vinegar and food-acid media in general, as dentifrices, appears to be devoid of harmful influences. Our study in this connection is in progress.

**119. The organic constituents of raw and burned soils.**  
ARTHUR W. THOMAS. Raw soil supplied through the kindness of

<sup>16</sup> Gies: *Proceedings of the Society for Experimental Biology and Medicine*, 1908, vi, p. 27. The apparatus referred to consists of a rectangular heavy-glass box, with an adjustable glass lid—in effect, a tall, rectangular box open at one broad side instead of at the top, and resting on the opposite side.

<sup>17</sup> Lothrop and Gies: *Journal of the Allied Dental Societies*, 1913, viii, p. 304.

Dr. F. J. Seaver, of the N. Y. Botanical Garden, was examined by the methods described on page 210. In each experiment 3 kilos of soil were treated with 9 liters of 2 percent sodium hydroxide sol. for 4 days. Slight traces of di-hydroxy stearic acid, resin acids, paraffins and paraffin acids, picoline carboxylic acid, arginin and histidin were found in the unburned soil.

Three kilos of this raw soil were then "burned" by placing them in an oven at 12 o'clock noon. The oven temperature rose from 100° to 150° C. by 5 o'clock and was kept at that point until 9 o'clock the next morning, when the soil was removed and treated in the same manner as the unburned portion, with the result that there seemed to be less di-hydroxy stearic acid, more resinous substances soluble in ether, and neither picoline carboxylic acid, histidin nor arginin. There appeared to be no change in the amount of paraffin compounds.

On the whole the work was quite unsatisfactory because of the fact that the isolated substances were too small in amount to be conclusively identified. The work has served to show, however, that one must start with many times the amount of soil recorded above in order to determine the changes in the chemical nature of the organic constituents of soils under the influence of heat.

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## BIOCHEMICAL BIBLIOGRAPHY AND INDEX

### 5. Fourth quarter, 1913 (October–December)

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Explanation of abbreviations, arrangement, notation, etc. BIBLIOGRAPHY. *Titles of papers* are freely shortened, minor words ignored, common terms conveniently abbreviated or chemical symbols substituted; *surnames* of collaborators are connected by hyphens; most *punctuation marks* are omitted—all for the sake of condensation. Heavy faced Roman numerals indicate *volumes*; heavy faced Arabic numerals designate *numbers and dates of issue* (slanting lines separate numerals for months and days). *Bibliographic items* begin with em dashes. When two or more papers by the same author occur together, they are duly numbered, and separated by semicolons, but follow the same em dash. Numerals preceding italicized names of authors indicate *sequence in the bibliography (index numerals)*; numerals preceded by commas, at the ends of items, indicate *initial pages of the corresponding papers*.

INDEX (SUBJECTS). The numerals in the index (page 320) correspond with the numbered items in the bibliography. *Pages are not indicated*. Numerals held in groups by hyphens are plain abbreviations in accord with the indications of the first numeral of each such series (see footnote, p. 320). Abbreviations of words in the index are similar to those in the bibliography. Each *group of index references* is terminated by a semicolon; commas mark off *subdivisions of a general index subject*. *Names of authors are not indexed*.

JOURNALS INCLUDED: *Biochemische Zeitschrift* (B.Z.), *Zeitschrift für physiologische Chemie* (Z.p.C.), *Journal of Biological Chemistry* (J.B.C.), *Biochemical Journal* (B.J.), *Biochemical Bulletin* (B.B.).

PRACTICAL USE OF THE BIBLIOGRAPHY. The bibliography is helpful from several standpoints. Thus, if it is desired to ascertain whether the journals included in the bibliography contain any papers (during the given quarter) on a particular subject, *e. g.*, lipins, find the key word in its alphabetical place in the index and turn to the items in the bibliographic sequence indicated by the index numerals (in this case 39, 84, 209, 435–43–9, 613–4–7–9). The abbreviated items thus identified give the names of authors and suggest the nature of the corresponding papers (ten papers in the case selected for illustration), and help the reader to decide whether to examine the original publications. When the index gives a negative answer to an inquiry, a large mass of literature is removed from further consideration. During the intervals between publication of the indexes of journals, *Zentralblätter* and year books, this running bibliography directs the reader to most of the main tracks through current literature on the leading biochemical subjects.



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<sup>1</sup> This series of abbreviations, illustrating all others in the index, represents the following sequence of numerals: 28, 415, 416, 443, 446. The numerals in bold-face type here are omitted from the abbreviations above.



thocyan89; anthozo213; antibod40,70; antig40,60,70,83; *Antirrhin-maj*602; appar442,701; As702; *Asperg-nig*441; autol29,88,441. B.-*Plymouth*208; bacter54,102,218-37,427,706; barm44; base35,423-37-47; beef708; benzo-ac425; benzol204,ring204; benz'alan704; benz'-comp225; bibliog-bioch718; bioch-new-note-com719; Bioch-Soc-Eng716; bl'd16,25,32-7,76,81,91-7,100,240,406-15-22-32-51,615,clot76,corp66,glycol's451,sug12,41,55,219; brain617; branch-cleft-org439; but'r436. CaSO<sub>4</sub>33; carbohy60,404; C3I,411,exch50; CO<sub>2</sub>235,406-42; CO605-6; carotin227; casein1,447; caseinog-clot612; cell14,87; cereb'sp-fl71; cereal48; chicory26; chitin207; chlor'hydr211; chlorid13; Cl16,81; chl'f'm11; chloroph147,63; cholest443,613,c-iso617; cholin228; *Cichor-inty*b26; clay85; clot76,100,612; cocoa77; codein69; cold-stor709-10; col'd2,13,29,31,80,87,96,C3I,precip2,S29; colorim75,705; compl-reac4; coprostanon614; coprosterol614-9; correct'n70; creatin239,413,603; cr'inin413,603; cr'tosin226. Deamid64; diabet41,95,429-38-52; dialys10; diast8,620; dibrom-tyros212; diet404-5,613,textur403; diges43,77,414-6-7; dihy'sphingos449; dioxyphen'-alan224; disinfect209; distrib25,201-28. Egg-alb609; emulsin94; enzym7,8,10,18,23,32,45,78,86,236,401-2-27-30-7,620-1,704,act'n610; ereps45; ery'cyt-strom39; esteras401-2; ether11; excr403-4-5; Exp-Sta717; extr'v226. Fast36,59,417; fat38,404-24-36-46,feed424; fat-ac3,435-40; fecal-bac706; fermt'n32,43,79,208-10-1; fever99; fish38,229,432-3,709-10,sperm216; flower-pig602; food41,208,709-10; form-ac208; formol-add14; fungi411-41,704; furf'ol210; furyltrimethylenglyc210. *Gadus-Brandt*i229; galactosid617; gall-ston227; gasomet408-9; globul607; glucon'gen452; glucosam54,102,207; glucos66,429; glucosid78; glucur-ac238; glycid438; glycin705; glyocol434; glycog92,620; glycol's65,95,451; glycosur214; glyoxylas444; gold-numb97; gold-sol96; grow21,230,418-36-7. Heat-balance99; heart25,49,freq82; hemin202-33; Hb605-6; hemolysing1,611; hemolys73,611; hex-bas447; histid75; humus703; hydant428; HCl601; H'conc71; H<sub>2</sub>S72; hydro1,9,601-20; OH85; hyp'glycem74,90,205-14. Inanit576; index-bioch718; indican206; indigo206; indol9; infect67-8; inf-ven-cav406; insect5,6,7; intes28,69; inulin-metab26; inv'tas18,236; I439,604; ioniz37; isocholest619. Kaolin85; kephal435; kidn450. Lac-ac95; lead33; PbSO<sub>4</sub>33; leaves24; leucocy73,450; *Leucocytoz-syph*608; lipas430; lipin(oid)39,84,209,435-43-9,613-4-7-9; lipoprot84; liv15,72,92,204-20,401-34-45. Maltas10,23,44-8,59,78; maltos19; "Mathews plan"720; meat-extr35,226; meio-stag-reac83; membran52; Hg-arom-comp'd53; mesohemin202; metab26,36,414-6-7-23-4-5-32,711-2; meth17,27,33-4,55-7,61,75,81,97,203-10-3-9-21-7-35,406-7-8-9-14-9-20-1-2-6-31-40-1,601-3-9-18-21-2-707-8; a-meth'glucosid78; micro-meth55,408-21-42; milk412-27; mold441,704; morph51,426; mucon-ac204; muscl95,226,413. Narcos30,52; nephelom421; nephrotox433; nerv223; new-not-com-bioch719; N71-7,229-34,403-4-5-8-14-23-4-5-31,702,retent234,subst77; nucl-ac232; nutrit59,67-8,230-1,403-4-5-17-23-4-5,613,711-2. Opium51; org-bas228; oxidas7; oxidat614; oxydon7;  $\beta$ -oxybut-ac419,22; O406,605-6,consump30. Paner232,445; pentosur101; peptol32; percin217; permeab66; phenol7,428; P21; phos'tid39,49; photoch46; pigm87,602; plant-cell87; plast'n22; polem17-8-9,35,57,80,214-5-22; polyat-alcoh411; polysacch621; precip2,35,80,609-16; pregn41; proc'd713-4-5; prolin1; prop-ac429; prop'ald452; prot'n9,14,71,84,96-7-8,203-16-23-5,405-14-5-6-7-48,601-7-22,dig-prod414-5-6-7; ptomain426; purin410-28,base35; pyrimid428; pyruv-ac618. Quad'urat222. Ra430; reductas86; reduc211; refrig709-10; regen8; renning93; resp5,6; rhamnosid201; rice418; root56; ruminant43. Sacchar62; salt13,33,234,418-23,620; separ33,407,622; ser11,37,59; NaF402; soil418,702; sperm

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## BIOCHEMICAL NEWS, NOTES AND COMMENT

### EDITORIAL SUB-COMMITTEE:

Walter H. Eddy, Alfred P. Lothrop,  
Paul E. Howe, Arthur Knudson.

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### I. GENERAL

**Necrology.** *W. Popplewell Bloxam*, formerly prof. of chemistry in Presidency Coll., Madras, author of papers on the production and chemistry of indigo.—*Frederick C. Busch*, for some years prof. of physiology at the Univ. of Buffalo, recently engaged in cancer research.—*Edwin Klebs*, pathologist and bacteriologist, for a year prof. of pathology in Rush Med. Coll., the first to describe *Bacillus diphtheriae*, "the last of the great pioneers of the bacterial theory of infection, a pupil of Virchow's, a contemporary of Pasteur and the inspirer of Koch."—*S. Weir Mitchell*, distinguished as a man of science, as a man of letters and as a physician.—*Louis Wickham*, founder of the Laboratoire biologique du radium, widely known for his researches on the value of radium in the treatment of cancer and other diseases of the skin.

**In memoriam.** The tablet unveiled at King's College by Lord Rayleigh, on Jan. 14, to the memory of Lord Lister bears the following inscription: In affectionate and respectful memory of Joseph Baron Lister, F.R.S., O.M., professor of clinical surgery in King's College from 1877–1892, and for many years consulting surgeon to the King's College Hospital, member of the council and life governor of the college, this tablet is erected. His name will be handed down to posterity as the founder of antiseptic surgery, one of the greatest discoveries in history, and a source of inestimable benefit to mankind.

**Honors.** AWARD OF PRIZES. *Nobel prizes*, for 1913: In medicine, to Dr. *Charles Richét*, prof. of physiology in the Univ. of Paris, director of the Inst. Marey, in recognition of his work on anaphylaxis; in chemistry, to Prof. *Alfred Werner* of the Univ. of Zurich.—The Paris Acad. of Med. has awarded the *Chevillion prize* of 1500 francs to Dr. *R. Robeison*, of Paris, for his account of a method of biochemical diagnosis of cancerous affections.—Awards of 1500 francs, each, have been made to *M. Marquis* for his memoir on mercuric chlorid in surgery, and to *F. Bezançon* and *S. L. de Jong*, for their treatise on the examination of sputa.—By recommendation of the commit. on the award of the *Hodgkins prize* of \$1,500, for the best treatise On the relation of atmospheric air to tuberculosis, which was offered by the Smithsonian Inst'n in connection with the Int. Cong. on Tuberculosis, in Washington (1908), the prize has been equally divided between Dr. *Guy Hinsdale*, Hot Springs, Va., for his paper on Tuberculosis in relation to atmospheric air, and Dr. *Adolphus Knopf*, New York City, for his treatise on the Relation of atmospheric air to tuberculosis.

AWARDS OF MEDALS. The special board for biology and geology at Cambridge Univ. has adjudged the *Walsingham medal* for 1913 to Mr. *Franklin Kidd*, fellow of St. John's, for his essay On the action of carbon dioxid in the moist seed in maturing, resting, and germinating conditions.

The Royal Society has awarded a *Royal medal* to Prof. *E. H. Starling* for his contributions to the advancement of physiology, and a *Davey medal* to Prof. *R. Meldola* for his work in synthetic organic chemistry.

The fourth annual award of the *Willard Gibbs Medal* will be made by the Chicago Sect. of the Amer. Chem. Soc'y to Dr. *Ira Remsen*, of Johns Hopkins University. The previous recipients of this medal are Prof. Svante Arrhenius, Prof. Theodore W. Richards and Dr. Leo H. Baekeland. The formal presentation will be made to Dr. Remsen at the May meeting of the Chicago Sect. of the Amer. Chem. Soc'y. Jury of award: Mr. William Brady, Mr. G. Thurnauer, Dr. E. C. Franklin, Dr. W. R. Whitney, Prof. J. H. Long, Prof. J. Stieglitz, Prof. Alexander Smith, Prof. W. A. Noyes, Mr. E. B. Bragg, Mr. S. T. Mather, Prof. W. H. Walker and Prof. T. W. Richards.

MEMBERSHIP IN THE COUNCIL OF THE ROYAL SOCIETY. Profs. *W. M. Bayliss* and *F. Gowland Hopkins* have been nominated for election to the Council of the Royal Society of London.

**Appointments.**<sup>1</sup> Canadian Gov.: Dr. *F. J. Birchard* (U. S. Dep't of Agric., Bur. of Chemistry), chemist to the Dep't of Trade and Commerce.

Carnegie Inst'n, Nutrition Lab. (Boston): Prof. *H. Monmouth Smith* (Syracuse Univ.), assistant.

Drexel Inst. of Art, Science and Industry: Dr. *Hollis Godfrey*, president.

Greifswald Hygienic Inst.: Prof. *Rocmer* (Marburg), director, to succeed Prof. *F. Loeffler*.

Harvard Univ.: Dr. *William Duane*, assis. prof. of physics; in charge of investigations of the physiological action of radio-active substances, at the Harvard Med. Sch. and the Huntington Cancer Hosp.

New York City Dep't of Health: Dr. *William H. Park*, chief executive of the Bureau of Laboratories, in the reorganization of the department.

N. Y. Univ. and Bellevue Hosp. Med. Coll.: Dr. *Ephraim M. Ewing*, assis. prof. of physiology.

Oregon Agric. Coll. (Corvallis): Dr. *R. A. Dutcher*, instr. in agric. chemistry.

Oxford Univ.: Dr. *C. S. Sherrington* (Univ. of Liverpool), Waynflete prof. of physiology, to succeed the late Dr. *Francis Gotch*.

Throop Coll. of Technology (Pasadena, Cal.): Mr. *Howard J. Lewis* (Ohio State Univ.), instr. in chemistry, vice Dr. *Chas. A. Brautlecht*, resigned.

Turck Inst. (N. Y.): Dr. *Robert Bengif* (Yale Univ.), assistant in a study of the chemistry of bacteria.

Univ. of Innsbruck: Dr. *Adolf Windaus*, prof. of chemistry.

Univ. of Kansas: Dr. *W. S. Long*, assis. prof. of chemistry, in charge of the food lab.; Dr. *C. F. Nelson*, assis. prof. of physiol. chemistry.

Univ. of Texas: Dr. *Henry W. Harper* (prof. of chemistry since 1894), first dean of the graduate Dep't.

Univ. of Utah, Med. Sch.: Dr. *L. D. Swingle*, assis. prof. of pharmacology.

West Va. Univ.: Dr. *Wm. Henry Schultz*, prof. of pharmacology and mat. medica; Dr. *Aaron Arkin*, prof. of bacteriology and pathology.

<sup>1</sup> In this summary institutions from which *resignations* occurred are named in parentheses. See pages 329 and 335.



**Grants.** BY THE PARIS ACADEMY OF SCIENCE, FROM THE BONAPARTE FUND. *Jean Pougnet*: 2,000 fr., for researches on the chemical and biological action of ultra-violet light; *Alphonse Labbé*: 2,000 fr., for researches on the modifications undergone by animals on changing from salt to fresh water, or the reverse.

**Research funds.** PRIZE FOR RESEARCH IN PHYSIOLOGY OR PHYSIOL. CHEMISTRY. A prize, to be awarded annually or biennially, for the best essay by local investigators on research in physiology or physiological chemistry, has been established at the University of Manitoba.

**SARAH BERLINER RESEARCH FELLOWSHIP FOR WOMEN.** The committee in charge of the Sarah Berliner Fellowship offers, annually, a fellowship of the value of one thousand dollars. It is available for study and research in physics, chemistry or biology, in either America or Europe, and is open to women holding the degree Ph.D., or to those similarly equipped for the work of further research. Applications for this fellowship should be sent to the chairman of the committee, Mrs. Christine Ladd-Franklin, 527 Cathedral Parkway, N. Y.

**COMMIT. ON SCIENTIFIC RESEARCH OF THE AMER. MED. ASSOC.** The committee on scientific research under the auspices of the Amer. Med. Assoc. has decided to use its new appropriation for the promotion of medical research where suitable conditions exist but where such work suffers for the lack of relatively small sums of money. Applications for grants are invited and may be sent to any member of the committee: Drs. *Ludvig Hektoen*, 1743 W. Harrison St., Chicago; *Simon Flexner*, Rockefeller Inst., N. Y., and *Wm. Litterer*, Vanderbilt Univ., Nashville, Tenn.

**Lectures.** **HERTER LECTURES.** Five daily lectures upon the Herter Foundation, on Colloids and their relation to biological chemistry, were delivered at the N. Y. Univ. and Bellevue Hosp. Med. Coll., Jan. 12-16, by Prof. *Sven G. Hedin*, of the Univ. of Upsala.

**HARVEY LECTURES.** January 17: The phenomena of infection, Prof. *V. C. Vaughan*, Univ. of Mich.—January 24: Colloidal reactions and their relations to biology, Prof. *Sven G. Hedin*, Univ. of Upsala.

PHI LAMBDA UPSILON LECTURE, COLUMBIA UNIVERSITY. December 18, 1913: The mechanism of biological utilization of sugars, Dr. *P. A. Levene*, Rockefeller Inst.

MISCELLANEOUS ITEMS. On January 8 Prof. *Theobald Smith* delivered a lecture on Prophylactic and therapeutic vaccines before the N. Y. State Veterinary Coll., at Cornell Univ.—Dr. *Adolph Schmidt*, prof. of internal medicine in the Univ. of Halle, and editor of the *Zent. für innere Med.*, was the guest of the Cincinnati Acad. of Med., Nov. 3, and delivered an address on internal diseases.

RUSH LECTURES. The Rush Society for the correlation and support of medical and biological lectures in Philadelphia announces the following lectures among others, which will be given at the Coll. of Physicians, or at the Medical Laboratories of the Univ. of Penn. Sixth Rush Society Lecture, January 27: Prof. *Sven G. Hedin*, Univ. of Upsala, Colloidal reactions and their relations to biology.—*Weir Mitchell Lecture*, February 25: *Harvey Cushing*, Harvard Univ., Clinical types of dyspituitarism.—Seventh Rush Society Lecture, March 11: *John Howland*, Johns Hopkins Hosp., A consideration of certain aspects of rachitis. (Also the annual address before the Alpha Omega Alpha Honorary Med. Soc'y.)—Eighth Rush Society Lecture, April 1: *Alexis Carrel*, Rockefeller Inst., Permanent active life of tissues outside of the organism. (Also the annual address before the Undergraduate Med. Soc'y of the Univ. of Penn.)

LEYDEN LECTURE. Prof. *Emil Abderhalden* delivered the Leyden lecture to the Soc'y of Internal Med., Berlin, on Serological diagnosis of organic changes.

Proceedings, and officers-elect, of societies, associations, etc.

AMER. ASSOC. FOR THE ADV. OF SCIENCE. See *Science*, 1914, xxxix, p. 39. Pres't: *Charles W. Eliot*; Vice-pres'ts: Section C (Chemistry), *Carl L. Alsberg*; Section F (Zoology), *Frank R. Lillie*; Section K (Physiol. and Exp. Med.), *Richard M. Pearce*.

MISCELLANEOUS ITEMS. Proceedings of the annual meetings of the societies named below are published, at the pages indicated, in this number of the BIOCHEM. BULL.: Amer. Physiol. Soc. (p. 282); Amer. Soc. of Biol. Chemists (p. 285); Amer. Soc. for Pharmacol.

and Exp. Therap. (p. 288); Amer. Soc. for Exp. Pathol (p. 290); Amer. Soc. of Naturalists (p. 296); Amer. Soc. of Zool. (p. 294); Amer. Assoc. of Anatomists (p. 297); Soc. of Amer. Bacteriologists (p. 299).

AMER. CHEM. SOC'Y: Pres't, *Theodore W. Richards*; directors, *M. T. Bogert* and *A. D. Little*; councillors-at-large, for a three-year period, *C. H. Herty*, *Julius Stieglitz*, *L. H. Baekeland* and *W. L. Dudley*.

AMER. PHYTOPATH. SOC'Y: Pres't, *Haven Metcalf*; vice-pres't, *Frank D. Kern*; member of council, *H. R. Fulton*; chief editors of *Phytopathology*, *L. R. Jones* (one year), *C. L. Shear* (two years), *R. A. Harper* (three years); assoc. editors (three years), *F. D. Heald*, *Mel T. Cook*, *B. M. Duggar*, *F. C. Stewart*; bus. manager of *Phytopathology*, *Donald Reddick* (reelected).

INTERN. CONGR. (IX) OF PHYSIOLOGY, Groningen, Sep. 2-5, 1913. See *Archiv intern. de physiol.*, 1913, xiv, pp. 1-84 (No. I.)

Miscellaneous items. AMER. JOUR. OF BOTANY. The *Amer. Jour. of Botany*, an official publication of the Bot. Soc'y of Amer., begins with the issue of January, 1914. It starts with the joint support of the Bot. Soc'y of Amer. (the national botanical society) and the Brooklyn Bot. Garden, and is open to publications in all branches of botanical science. The board of editors comprise five appointed by the Soc'y: Profs. *F. C. Newcombe*, ed.-in-chief, Univ. of Mich.; *R. A. Harper*, Columbia Univ.; *R. L. Jones*, Univ. of Wis.; *G. T. Moore*, Mo. Botan. Garden; *D. S. Johnson*, Johns Hopkins Univ., and two appointed by the Brooklyn Bot. Garden: Drs. *C. Stuart Gager*, bus. manager, and *E. W. Olive*. The new journal will be published monthly, except during July and August. The subscription price is \$3.00 a year to members of the Bot. Soc'y of Amer.; to all others \$4.00.

CENSORSHIP COMMIT. FOR THE BUREAU OF CHEMISTRY. A censorship committee, consisting of Dr. *C. S. Hudson*, Dr. *I. K. Phelps*, Dr. *H. A. Seil*, Dr. *A. L. Winton*, chairman, and Mr. *W. D. Collins*, secretary, has been appointed for the Bureau of Chemistry. Hereafter all manuscripts intended for publication by officers of the Bureau must be submitted for criticism to this committee. The

recommendations of the committee may be overruled by the Chief of the Bureau.

**SIXTH SESSION OF THE GRADUATE SCH. OF AGRIC.** The sixth session of the Grad. Sch. of Agric. will be held at the Coll. of Agric. of the Univ. of Missouri, beginning June 29, 1914, and continuing four weeks. All correspondence relating to membership in this school should be addressed to *A. J. Meyer*, Registrar, Coll. of Agric., Univ. of Missouri, Columbia, Mo.

**SANITARY COMMITTEE FOR CHICAGO.** Profs. *Julius Stieglitz* (Univ. of Chicago), *John H. Long* (Northwestern Univ.), and *Harry McCormack* (Armour Inst. of Tech.), are members of a commit. appointed by the Chicago sect. of the Amer. Chem. Soc'y to cooperate, if desired, with the mayor of Chicago in the solution of the city's waste problem.

**SCHOOL FOR THE STUDY OF SUGAR.** The Natal Sugar Growers' Assoc. has recently established, in connection with the Durban Tech. Inst., a school for the study of sugar. Their support involves the establishment of lectureships in chemistry, bacteriology and entomology, and the funding of researches on the manufacture and growing of cane sugar.

**PRIESTLY'S BALANCE.** The descendants of Priestly, the discoverer of oxygen, have presented to the Univ. of Penn. the chemical balance which was used by him in his experiments.

**SILLIMAN LECTURER.** Dr. *J. S. Haldane*, reader in physiology at Oxford Univ., has been chosen Silliman lecturer at Yale Univ.

**BERNARD CENTENARY.** The centenary of the birth of Claude Bernard was celebrated at the College de France on December 30.

## II. COLUMBIA UNIVERSITY BIOCHEMICAL ASSOCIATION

### I. General notes

**Marriage.** On Dec. 15, Miss Rahil Wattman and Dr. Max Kahn.

**Appointments.** Dr. *Sidney Born*, chief chemist of the Lemp Brewing Co., St. Louis.—Dr. *George A. Geiger*, assis. chemist, Bureau of Chemistry, U. S. Dep't of Agric.—Dr. *A. J. Goldfarb*,



assis. prof. of natural science, Coll. of the City of N. Y. (promotion).—Dr. *Isidor Greenwald* (Montefiore Home Lab.), assistant, Harriman Research Lab., Roosevelt Hosp. (N. Y.).

**Officers-elect of societies.** Dr. *Carl L. Alsberg*, vice-pres't, Sect. C (chemistry), Amer. Assoc. for the Adv. of Science.—Prof. *Isabel Bevier*, member of the Board of Trustees of the Ellen Richards Home Economics Fund for Research and Publication.—Dr. *A. Richard Bliss*, historian and editor, Kappa Psi Med. Fraternity (re-elected).—*Helen Gavin*, cor. sec'y, N. Y. Assoc. of Biology Teachers.—Prof. *Hugo Kronecker*, member of the Gen'l Commit. of the Ninth Intern. Congr. of Physiology, convened in Groningen last September.—Dr. *Raymond C. Osburn*, vice-pres't and chairman of the sect. of Biology, N. Y. Acad. of Sciences.—Dr. *William A. Taltavall*, treas., San Bernardino Co. (Cal.) Med. Soc'y.

**Members-elect of societies.** *Ross A. Gortner*, Amer. Soc. of Naturalists.—*Harold M. Hays*, Amer. Coll. of Surgeons (fellow).—*Edward C. Kendall*, Amer. Soc. of Biol. Chemists.—*Wilbur Ward*, Amer. Coll. of Surgeons (fellow).

**Lectures.** Dr. *Jacques Loeb* conducted the thirty fourth annual course, at Richmond Coll., Va., under the James Thomas lecture endowment, Dec. 11 and 12. The first lecture was on Artificial parthenogenesis; the second, on Determinism in the animal world. At the regular fall meeting of the Chicago chapter of the Soc'y of the Sigma Xi, Dec. 1, Dr. Loeb spoke on Recent experiments in artificial parthenogenesis.

Under the auspices of the local chapters of the Soc'y of the Sigma Xi, Prof. *Lafayette B. Mendel* gave a "popular" lecture on Food fads, also a more technical lecture on View-points in the study of growth, at the Univ. of Kansas, Lawrence (Dec. 1 and 2), at the Univ. of Missouri, Columbia (Dec. 3 and 4), and at Washington Univ., St. Louis (Dec. 5 and 6). He was entertained at each of these places by the local chapters of Sigma Xi or by members of the faculties of the institutions, and gave additional informal talks on educational or scientific topics at each of the universities.

**Miscellaneous items.** The first edition of A laboratory manual of qualitative chemical analysis for students of medicine, dentistry



and pharmacy, by Dr. *A. R. Bliss*, prof. of chemistry and pharmacy, and director of the chemical and pharmaceutical laboratories, in the Birmingham Med. Coll. and Graduate Sch. of Med., Univ. of Ala., has just left the press.

Miss *Jean Broadhurst* and Dr. *Ernest D. Clark* have been re-elected assoc. editors of *Torreya*.

The following statement is the concluding sentence in the preface of Prof. W. A. Bastedo's *Materia medica: pharmacology: therapeutics: prescription writing; for students and practitioners* (1913): "For the use of a number of tracings I owe my deepest thanks to my colleague, Dr. *Charles C. Lieb*, whose care about the details of an experiment and accuracy in recording results I believe to be unsurpassed."

## 2. Proceedings of the Association

**Third annual dinner.** The third annual dinner of the Biochemical Association was held at the Hotel Marseilles, Broadway at 103rd Street, on Friday evening, November 21, 1913. About one hundred and forty members and their guests were present and enjoyed the informal reception which preceded the dinner. The dinners of the Association have been increasingly more enjoyable, and they occupy a very important place in the activities of the Association. One of the factors which added greatly to the pleasure of the occasion was the opportunity afforded, especially to the younger members, of meeting so many men who have made notable contributions to biological chemistry and to other fields of research closely related to it.

Prof. Lafayette B. Mendel of Yale University was the guest of honor. The president, Prof. Stanley R. Benedict of the Cornell University Medical School, was the toastmaster. Prof. Charles Baskerville, Prof. M. A. Bigelow, Dr. C. B. Davenport, Dr. Charles A. Doremus, Dr. P. A. Levene, Dr. Samuel J. Meltzer and Prof. Henry C. Sherman addressed the Association informally. Professor Mendel discussed some of the results of his recent investigations on "Growth"; the address is published in this number of the *BULLETIN* at page 156.

Dr. Walter H. Eddy presented Professor Mendel's name for

election to honorary membership in the Association; the nomination was seconded by Dr. Ross A. Gortner. Prof. Mendel was unanimously elected by a rising vote of the members present.

The names of those present and the table groupings are indicated below.

### *Speakers' Table*

*Charles Baskerville	*James Ewing	Lafayette B. Mendel
*S. P. Beebe	*Cyrus W. Field	*T. H. Morgan
Stanley R. Benedict	*Robert A. Harper	*†J. R. Murlin
*M. A. Bigelow	*P. A. Levene	*†Charles Norris
*Marston T. Bogert	†Jacques Loeb	*William H. Park
*†E. G. Conklin	*Graham Lusk	*Jean Perrin
*Charles B. Davenport	*Wm. G. Lyle	*H. C. Sherman
*Charles A. Doremus	*F. H. McCrudden	*F. C. Wood
	*S. J. Meltzer	

\*W. A. Bastedo  
Wm. B. Boyd  
T. Stuart Hart  
\*D. S. D. Jessup  
\*I. Levin  
†R. Burton-Opitz  
\*E. E. Smith  
\*Fenton B. Turck  
\*Wm. R. Williams

\*Jerome Alexander  
\*James P. Atkinson  
\*John Auer  
\*Edwin J. Banzhaf  
J. G. M. Bullowa  
\*K. George Falk  
\*Walter A. Jacobs  
\*Philip Adolph Kober  
Gustave M. Meyer  
\*†Victor C. Myers  
\*H. T. Vulté

A. M. Buswell  
\*Mrs. A. M. Buswell  
\*Mary Louise Landon

\*Guest.

† Detained or obliged to leave before the conclusion of the dinner.

Jean Broadhurst  
\*Louisa Bruckman  
Helen Gavin  
\*Mabel L. Gies  
\*Harriet R. Howe  
\*Maud O. Jessup  
Hildegard Kneeland  
Marguerite T. Lee  
Emily C. Seaman  
\*Caroline E. Stackpole

\*Katherine R. Coleman  
\*Morris S. Fine  
\*Martha F. Hilditch  
\*Warren W. Hilditch  
\*Alma K. Kleiner  
\*Israel S. Kleiner  
\*Robert C. Lewis  
Grace MacLeod  
\*Mary Swartz Rose  
Anton R. Rose

J. Garfield Dwyer  
†Donald Gordon  
\*W. H. Haskin

\*Ann L. Martin  
 Percy W. Punnett  
 Jessie Moore Rahe  
 \*A. H. Rahe  
 \*Mildred D. Schlesinger  
 Arthur W. Thomas  
 Jennie A. Walker

O. C. Bowes  
 \*Duncan Mac T. Fuller  
 S. Kubushiro  
 \*B. F. Rankin  
 \*†C. J. Snyder  
 \*P. Carter Speers  
 Grover Tracy  
 John I. B. Vail.

Sidney Born  
 Ruth S. Finch  
 Harry L. Fisher  
 Ross A. Gortner  
 Isidor Greenwald  
 Tula L. Harkey  
 \*J. Arthur Harris  
 Arthur Knudson  
 Alfred P. Lothrop  
 Ethel W. Wickwire

\*Jacob Diner  
 \*D. J. Edwards  
 \*C. Z. Garside  
 Samuel Gitlow  
 Benjamin Horowitz  
 Paul E. Howe  
 Sergius Morgulis  
 \*R. H. Nicholl  
 \*Leo Roth  
 Hardolph Wasteney

Robert Bersohn  
 B. G. Feinberg  
 Wm. J. Gies  
 A. Gross  
 I. J. Kligler

Walter M. Kraus  
 Herman O. Mosenthal  
 †Ralph G. Stillman  
 †Oscar M. Schloss  
 †Herbert Wiener

\*Annie C. Bellows  
 Lucy H. Gillett  
 Hattie L. Heft  
 \*Anna F. Lounsbury  
 \*Catherine J. MacKay  
 Helen McClure  
 \*Mildred Martin  
 Margaret B. Stanton  
 \*Susan F. West

\*Bertha C. Avery  
 \*Hatty Dahlberg  
 Greta Gray  
 \*Joan Hamilton  
 \*A. Grace Johnson  
 \*Mary E. Pillsbury  
 Ethel Ronzone  
 \*Elizabeth Selden  
 \*Edna Walls  
 \*Eleana F. Wells

Harvey B. Clough  
 Walter H. Eddy  
 Fred W. Hartwell  
 Joseph S. Hepburn  
 Chester A. Mathewson  
 Hermann J. Muller  
 \*George T. Palmer  
 Matthew Steel  
 Edgar F. Van Buskirk  
 Charles A. Wirth

V. E. Levine  
 †Wm. A. Perlzweig  
 A. V. Salomon  
 Charles Weisman

\* Guest.

† Detained or obliged to leave before the conclusion of the dinner.

The arrangements for the dinner were in charge of a committee consisting of Dr. Walter H. Eddy, chairman, Prof. Paul E. Howe and Dr. Alfred P. Lothrop.

**Fourteenth meeting.** Abstracts of the communications which constituted the scientific proceedings of the meeting on Dec. 5, 1913, are given at page 303.

**Ostwald lectures.** At the suggestion of the Exec. Commit. of the Biochem. Assoc., Columbia Univ. invited Dr. *Wolfgang Ostwald*, Privatdozent at the Univ. of Leipzig, editor of the *Kolloid-Zeitschrift* and *Kolloidchemische Beihefte*, to deliver, at Columbia Univ., the series of lectures indicated below:

MONDAY, JAN. 19, *Havemeyer Hall*: What are colloids?; elements of qualitative colloid analysis; formation and preparation of colloids.

TUESDAY, JAN. 20, *Havemeyer Hall*: Mechanical, optical, electrical, and chemical properties of substances in the colloid state; classification of the colloids.

WEDNESDAY, JAN. 21, *Coll. of Physicians and Surgeons*: Changes in the colloid state; internal changes of state, swelling, setting, syneresis, adsorption, coagulation, peptisation.

THURSDAY, JAN. 22, *Havemeyer Hall*: Scientific applications of colloid chemistry.

FRIDAY, JAN. 23, *Havemeyer Hall*: Technical applications of colloid chemistry.

Each of the lectures was attended by an unusually large and attentive audience.

A similar series of lectures was delivered by Dr. Ostwald at each of the following institutions: Univ. of Cincinnati, Jan. 5-11; Univ. of Ill. (Urbana), Jan. 12-17; Johns Hopkins Univ., Jan. 26-31.

Before returning to Leipzig, Dr. Ostwald will probably deliver lectures on colloid chemistry at the Univs. of Chicago, Nebraska and Kansas, at McGill Univ., and before chemical societies in Washington and Indianapolis.

**Fifteenth meeting.** OSTWALD SMOKER AND RECEPTION. The members of the Assoc. had the privilege of meeting Dr. Ostwald, as their guest, at a smoker in the library of the Coll. of Phys. and Surg., on the evening of Jan. 23. Dr. Ostwald addressed the Assoc. informally, after Dr. Gies had expressed, for the members, the pleas-

ure they derived from meeting Dr. Ostwald and the gratification his very interesting and instructive lectures afforded them. The smoker was notably enjoyable because of the geniality of the guest, the large attendance, and the complete informality that prevailed. The members will retain very happy recollections of Dr. Ostwald's personality. —*Alfred P. Lothrop, Secretary.*

### 3. Columbia Biochemical Department

**Appointments to the staff.** Dr. *Charles Weisman* and Mr. *Victor E. Levine* have been appointed assistants.

**Members-elect of societies.** Amer. Chem. Soc'y: Messrs. *Arthur Knudson* and *W. A. Perlzweig*; Amer. Physiol. Soc'y: Prof. *Paul E. Howe*; Amer. Soc'y of Biol. Chemists: Dr. *Walter H. Eddy*.

**Overcrowded condition of the P and S laboratory.** The number of students taking "medical-elective" and graduate courses in the main laboratory at the Coll. of Phys. and Surg. is so large that it has been impossible to accommodate all who have applied for admission.

**Miscellaneous items.** Dr. *Benjamin Horowitz* has been appointed assis. prof. in physiol. chemistry at the medical school of Fordham University, N. Y.

Dr. *Walter M. Kraus* has begun a term of service as interne at Bellevue Hosp.

Dr. *Walter H. Eddy* recently lectured before the biology sect. of the N. Y. High Sch. Teachers' Ass'n on the Chemistry of photosynthesis, and before the graduate class in biological methods of teaching at Teachers' Coll., on Commercial biology and its teaching. Dr. Eddy has been appointed a member of the commit. to prepare a syllabus on the teaching of commercial biology in N. Y. City high schools; he is also a member of the Commit. on Biology of the National Educ. Ass'n, a sub-commit. of the Commit. on Articulation, which will revise the high school courses in biology in the U. S.

Professor *Gies* was elected an honorary member of the First District Dental Soc'y of the State of N. Y. at its meeting in the N. Y. Acad. of Med., on Jan. 5. At this meeting he opened the discussion of a paper by Dr. *Harvey W. Wiley*, on Dental drugs and



nostrums. He was also one of the speakers at the society's annual dinner, at the Hotel Astor, on Jan. 24.

**Summer session courses.** The usual courses in nutrition will be given next summer by Prof. Gies, Dr. Seaman, and associates, in the laboratories at the Coll. of Phys. and Surg. and at Teachers College. The laboratory at the Coll. of Phys. and Surg. will be open for research throughout the summer session.

## EDITORIALS

We present, on pages 276–293 of this issue, a general account of the proceedings of the first annual meeting of the Federation of American Societies for Experimental Biology and Medicine.

**Federation of Amer. Soc. for Exper. Biol. and Medicine** The origin of the influences which led to the establishment of the Federation may be traced farther back than the meeting of the American Physiological Society, in 1907, to which Professor Carlson refers on page 276. When it was formally proposed by Professor Abel, in the fall of 1906, to organize a biochemical society, the suggestion was vigorously opposed by a number of leading biological chemists who were also members of the Physiological Society. They urged that instead of organizing a biochemical society, the Physiological Society be reorganized on a foundation to include a biochemical section. A few biological chemists also urged that the idea of establishing a biochemical society be abandoned and that biochemists be effectively organized in the Biological Section of the American Chemical Society. These counter-proposals were rejected by the large majority of the biological chemists concerned, many of whom, with Professor Abel, were members of the Physiological and Chemical Societies. Their general views were voiced formally by Professor Abel, at the meeting for the organization of the Biochemical Society in New York, in 1906, when he said:<sup>1</sup>

I take the liberty of rehearsing briefly the reasons for which this meeting has been called. . . . We have become convinced that there is need in this country for an organization which shall further the interests and foster the growth of biological chemistry. Biological chemists at present are affiliated with widely differing societies and come little in contact with the great body of men who are interested in biochemical work. Whether we as chemists have as our field of work the physiological chemistry of our medical schools or deal with the chemical

<sup>1</sup> *Proceedings of the American Society of Biological Chemists*, 1907, i, p. 2; *Science*, 1907, xxv, p. 140.

problems of botany, zoology, pathology, pharmacology or medicine, we all have one common meeting-ground, and that is chemistry as applied to animal or vegetable structures, living or dead. As distinguished from the work of pure chemists, organic or inorganic, our efforts are directed towards throwing light on the life processes and functions of living structures, with the help of chemical and physico-chemical methods.

Now, it will be granted, I think, that scattered and divided forces cannot develop that coordination of effort that is desirable when many workers have one great interest in common. In such a case, organization is beneficial. It encourages research, it furnishes the mechanism for competent criticism and helpful discussion; and lastly, the very fact that we have felt impelled to organize will make it evident to faculties of science and medicine and to scientific and medical societies that a great and growing department of research demands its fitting place in the general scheme of higher education.

I come now to the question of an academic career in biological chemistry. You have probably all, at one time or another, been asked to recommend some young man for a teaching position in physiological chemistry. The authorities in question want a man who has had a first class training in organic, inorganic and physical chemistry and biology, has had some experience in teaching physiological chemistry, has an agreeable personality, is a fascinating lecturer, and a promising if not already fruitful investigator. For such a rare combination of natural endowment and acquired culture, there is offered a salary ranging from \$800 to \$1,500, the title of assistant or instructor, with guarded hints as to promotion at some uncertain date and still more non-committal statements as to a possible rise in salary.

Biochemical research is quite the thing to-day. Every species of laboratory, clinical, bacteriological, hygienic, pathological, pharmacological, wants a chemist. All these laboratories no doubt afford fine opportunity to the young chemist for training in the broad field of biological chemistry. But what of his future? Is it as promising as it should be?

This state of affairs is largely our own fault. We attend only the meetings of societies of other specialists for fear we shall lose something that lies on the border line between their territory and ours. These other specialists have their house in order, organization has done its invaluable service for them, and the result is that every worker knows his fellows, each knows where to turn for advice and sympathy;

each member, no matter how remotely placed or how depressing his immediate environment, has the courage and enthusiasm in his work which comes from being connected with those who have the profound conviction that their branch is one of prime importance and dignity.

I believe in special societies for specialists and I have no fear of the so-called narrowing influence of specialization. I feel rather that any possible danger in that direction is more than offset by the stimulus to go deeply into our subject which comes from association with those of like interests. Chemistry, the fundamental science that must always guide our work, offers unlimited opportunity for broadening the mind.

It is my firm conviction that a national society of biological chemists should be organized at once. There are in this country, as near as I can ascertain, about one hundred active workers in this field, using the term in its widest sense. A very small minority of those with whom I have corresponded are undecided as to the wisdom of forming such a society, but are willing to accept the action of the majority. Some of these, again, have raised the question as to the advisability of asking the Physiological Society to give us a separate chemical section.

Many of us have given careful thought to this proposition, but have decided that it will be best to have an independent organization. I have already outlined some of the advantages that would follow on organization, and I can only repeat that I believe these advantages would be greater if in name and fact the organization is independent. I believe that we can have a society on broader lines than is possible to a mere section. We wish to draw into our society the biological chemists of all departments of biology including those organic and physical chemists who take a lively interest in our subject, but who would perhaps not care to join a physiological society. In fact, since a large number of our proposed membership are primarily chemists rather than physiologists, we should be marching under a wrong banner, no matter how great the freedom granted by the parent society.

This desire for, or prejudice, if you will, in favor of, entire independence in name and action, would equally forbid our organization as a section under the American Chemical Society. While recognizing that the various branches of science are mutually dependent and constantly receiving help from each other we still contend that special devotion in each individual branch alone insures success. In other words, we should stand for *independence* with *interdependence*.

The first scientific meeting of the Biochemical Society was held



in Washington, in May 1907. The Secretary of the Biochemical Society, with the approval of the officers of the societies concerned, proposed and arranged for joint sessions of the Biochemical Society with the American Physiological Society and with the Washington section of the American Chemical Society, thus emphasizing the principle of "*independence with interdependence*" which animated the founders of the Biochemical Society. It was freely suggested, and the hope was often expressed at that time, that such joint sessions between naturally affiliated societies might lead to co-ordinated meetings annually and to the development of a working agreement to that end, thus securing all the scientific and professional advantages of "*independence with interdependence*" to which Professor Abel referred in the address from which the foregoing quotation is taken. The Biochemical Society, which had insisted upon a professional career of its own, was eager to show, nevertheless, that independence meant nothing more than individuality, *i. e.*, professional freedom—that it desired to work effectively with similar individuals in concerted efforts for the advancement of biological science.

The joint sessions in Washington (May, 1907) were so successful and agreeable, that the Secretary of the Biochemical Society, with the approval of the officers of all the societies concerned, proposed and arranged a few months later for joint sessions in Chicago, in December 1907, of the Biochemical Society with the American Physiological Society and the Biological Section of the American Chemical Society in affiliation with Section C (Chemistry) of the American Association for the Advancement of Science. The Secretary of the Biochemical Society was also Secretary of Section K (Physiology and Experimental Medicine) of the American Association for the Advancement of Science. He arranged for joint sessions (during the same week) of Section K with the American Physiological Society and the Society of American Bacteriologists, thus laying further emphasis upon the attitude of the officers of the new Biochemical Society in the matter of affiliation with other societies for the attainment of similar objects.

The success of the joint sessions at the Chicago meetings was a popular theme for informal discussion among those in attendance. The action of the Physiological Society, to which Professor Carlson



refers (page 276), was a product of the fermentation which the successful joint sessions had caused. Joint sessions between the Biochemical and Physiological Societies have been features of the annual programs ever since.

The Pharmacological Society was organized in Baltimore, in December 1908, by active members of the Physiological and Biochemical Societies, and Professor Mathews' plan for the organization of an American Biological Society, which was presented to the Physiological Society at that time, was received, filed and forgotten (p. 277).

Annual meetings of the Physiological, Biochemical and Pharmacological Societies, at the same time and place (with successful joint scientific sessions, and delightful smokers and dinners a recurrent feature), have kept the idea and desirability of *federation* prominently to the fore.

It was apparent, however, during the period from 1908 to 1911 inclusive, that influential members of the Physiological Society entertained the hope that the Physiological, Biochemical and Pharmacological Societies might be merged into a greater Physiological Society. During the annual meetings in Baltimore, in 1911, this hope was so frankly, openly and effectively stated that dissenting biochemists, among them founders of the Biochemical Society, made it evident, with equal candor and force, that such a plan would not be consummated if they could prevent it. Referring editorially to this matter two years ago we said, generally but none the less earnestly:<sup>2</sup>

THE BIOCHEMICAL BULLETIN is an ardent believer in biological chemistry as a science and an earnest advocate of it as a profession. We favor the continued independent existence of the American Society of Biological Chemists. Any movement intended to effect a merger of the American Society of Biological Chemists with any other organization to the detriment of biological chemistry as a profession would be opposed openly and candidly on these pages. . . . Five years ago when the American Society of Biological Chemists was organized, Professor Abel made a satisfying public statement of the reasons why biological chemists should perfect an independent professional organization. We commend Professor Abel's statement now to the attention

<sup>2</sup> Editorial: BIOCHEMICAL BULLETIN, 1911, i, p. 364.

of all who may be interested in seeking the dismemberment of the national Biochemical Society. (This statement by Prof. Abel is quoted on p. 337).

During the informal conferences at the Baltimore meetings, in 1911, it was repeatedly suggested by the biochemists, to those who wished to bring about absorption of the Biochemical Society into the Physiological, that a biological federation be organized, and that such a federation be made in effect a biological society in which the constituent organizations could coöperate *without loss of name or autonomy*. The rapid evolution of the Biochemical Club of England, into the Biochemical Society of England,<sup>3</sup> offered sufficient further encouragement to American biochemists, in their stand against a merger of the Biochemical Society into another organization, to make such an event wholly impossible. The "eat 'em alive" physiologists in this country dropped the discussion of "absorption." Federation was substituted for assimilation. The federation idea grew into unanimous acceptance. Within the year, in Cleveland in 1912, federation was formally ratified. A few weeks ago, at Philadelphia, federation became a reality.

The four constituent societies in the Federation are now affiliated, in "*independence with interdependence*," on a basis of equality and mutual respect, and in fraternal accord, for the attainment of similar scientific and professional ends. The Federation is in effect an "American Biological Society," with splendid possibilities of growth in professional efficiency, in scientific service and in public influence.

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The career of the American Physiological Society has been a distinguishing feature in the history of science in America. The Physiological Society placed before "generations" of biochemists, pharmacologists and pathologists the highest ethical and professional standards, and set a stimulating example of scientific endeavor and achievement. The unqualified success of the Physiological Society, from its organization in 1887, has made possible the subsequent careers of the Biochemical and Pharmacological Societies, of which it is, in fact, the parent organization. The Federation, certain to follow the leadership of the Physiological Society,

<sup>3</sup> Halliburton: BIOCHEMICAL BULLETIN, 1911, i, p. 484; 1912, ii, p. 128.

may be relied upon to carry the standards of professional and scientific effort and efficiency farther forward toward ideal attainment than ever.

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For the purpose of recording further "inside" evidence on the sentiment of the constituent societies, as they entered the Federation, we present additional details on a point referred to by Dr. Auer, which is stated by him, on p. 279, as follows:

Another regulation was one designed to aid in the administration of the Federation affairs if the chairman and secretary of the executive committee<sup>4</sup> should be retired. The motion provides that the chairman and secretary of the executive committee, in the event of retirement from office in their society, become members of the executive committee for the ensuing year but in an *advisory* capacity only. The committee will thus always enjoy the advice of the chairman and secretary of the preceding year, *but there is no danger that one society will have at its disposal four votes out of ten in the deliberations of the executive committee of the Federation.*

This "regulation" in its original form, as ratified first by the Physiological Society, gave to the retiring "chairman and secretary of the executive committee, in the event of retirement from office in their society," full voting privileges on any question that might come before the executive committee, thus making it possible, on occasion, for one society of the four to exercise a disproportionate numerical influence in the deliberations of the executive committee. The resolution, when presented to the Biochemical Society for consideration, was at once amended into the final form in which it appears in Dr. Auer's account (quoted above). The Federation approved the regulation as amended, which insures an equal maximum number of votes in the executive committee for each of the four constituent societies. This action emphasized, in unmistakable terms, the *equality* (and *independence*) of the constituent societies.

Dr. Auer's account presents a special illustration of the prevail-

<sup>4</sup> The reader may recollect that the president and secretary of the presiding society are chairman and secretary, respectively, of the executive committee of the Federation. The societies preside regularly in this rotation: Physiological, Biochemical, Pharmacological, Pathological.

ing sentiment of "independence of the societies forming the Federation" (p. 280). The concluding paragraph of Dr. Auer's statement is a particularly apt expression of this spirit.

The "Mathews plan for the organization of an American Biological Society" was informally discussed freely by members of the biological societies at the Philadelphia meetings.<sup>1</sup> The Zoological Society formally referred the plan to its Executive Committee (p. 295). There seemed to be a general disposition to "await developments in the Federation," before attempting to proceed further with a central organization.

The substitution of analogy for fact is the bane of chemical philosophy; the legitimate use of analogy is to connect facts together and to guide to new experiments. *Davy.*

**Stimulants** Science is forever changing. The work of to-day is contradicted to-morrow. Few indeed are so fortunate as to leave in the permanent remembrance of science conclusive work. *Mitchell.*

The later life of the merchant and the lawyer loses vitality of normal interest as age comes on; not so with the man of science. The eternal love of nature is his—a mistress of unfading charm. *Bryce.*

The great mind resists. The quality of genius is rebellious. Did you ever hear of a *conforming* genius? Did any one ever win fame, except in the form of infamy, by *submitting*? Does the world echo with the name of a single great Acceptor? *Chamberlin.*

No professional man thinks of giving according to measure. Once engaged, he gives his best, gives his personal interest, himself. His heart is in his work, and for this no equivalent is possible; what is accepted is in the nature of a fee, gratuity, or consideration, which enables him who receives it to maintain a certain expected mode of life. The real payment is in the work itself—this, and the chance to join with other members of the profession in guiding and enlarging the sphere of its activities. *Pratt.*

<sup>1</sup> Eddy: BIOCHEMICAL BULLETIN, 1913, iii, p. 134.



## BOOKS RECEIVED

The BIOCHEMICAL BULLETIN promptly acknowledges here the receipt of publications presented to it. Reviews are matter-of-fact statements of the nature and contents of the publications referred to, and are intended *solely to guide possible purchasers*; the wishes or expectations of publishers or donors of volumes will be disregarded, if they are incompatible with our convictions regarding the interests of our colleagues. *The sizes of the printed pages are indicated, in inches, in the appended notices.*

**Artificial parthenogenesis and fertilization.** By Jacques Loeb, memb. of the Rockefeller Inst. Originally translated from the German by W. O. Redman King, assis. lecturer in zoology, Univ. of Leeds, Eng.; supplemented and revised by the author. Pp. 312— $6\frac{1}{4} \times 3\frac{3}{4}$ ; \$2.50 net. Univ. of Chicago Press, 1913.

A presentation, in the author's accustomed masterly manner, of the "methods by which the unfertilized egg can be caused to develop into an embryo and the conclusions which can be drawn concerning the mechanism by which the spermatozoon produces this effect." The voluminous mass of facts recorded and discussed by the author not only supports his theory that at least two factors are involved in this process—one ("essential") which induces a change in the *surface* of the egg; a second which is "corrective"—but also relates to such problems as the "natural death of the ovum and the prolongation of its life by fertilization; the fertilization of the egg by foreign blood and the immunity of the egg to blood of its own species; the relations between heterogeneous hybridization and artificial parthenogenesis, between fertilization and cytolysis, and between permeability and physiological efficiency of acids and bases." Gies.

**Materia medica: pharmacology: therapeutics: prescription writing.** By Walter A. Bastedo, assoc. in pharmacology and therapeutics, Columbia Univ. Pp. 602— $7 \times 4$ ; \$3.50. W. B. Saunders Company, Phila., 1913.

The work is divided into three sections. *Part I* serves as a general introduction and is especially commendable for the excellent discussion of the constituents of organic drugs. *Part II* deals with the individual remedies, which are considered on Schmiedeberg's plan. The discussion of the action and uses of the cathartics is unusually practical and valuable. The forty odd pages devoted to an explanation of the action of digitalis is justified by the importance of the drug and by the great increase in our knowledge of cardiac physiology and therapeutics. The action of digitalis is discussed in an original way, which makes more easy the apprehension of the complex action of this drug. The changes in the circulation are taken up according to the action on the sinus node, the cardiac muscle, the A-V bundle, the coronary and the systemic arteries. The action on each structure is first studied separately and the combined effects are then made clear. The numerous polygraphic tracings accompanying this chapter are unusually good, but it seems unfortunate that they are not elucidated by diagrams. The section dealing with the general anesthetics is also worthy of note. *Part III*, devoted to prescription writing, is short but comprehensive. Enough Latin grammar is given to facilitate prescription writing for those who have not studied Latin. The pages devoted to practice in prescription writing will prove a boon to students and teachers. It is to be regretted that preference is given throughout the book to the apothecaries' system of weights and measures rather than to the metric system. There are, as is to be expected in a first



### Books received (con.)

edition, numerous typographic errors. Some of these are most unfortunate, especially the confounding of grains and grams. To add to the confusion, the grain doses are expressed in Arabic figures instead of in Roman and many of the grain fractions are written as decimals. The suggestions as to treatment are conservative and are based on laboratory research as well as on clinical experience. The author has succeeded in his attempt to emphasize the value of research, both in the laboratory and at the bedside, and he pleads for a more scientific, and therefore a simpler, therapy. Lieb.

**Lehrbuch der physiologischen Chemie in Vorlesungen. I Teil: Die organischen Nahrungsstoffe und ihr Verhalten im Zellstoffwechsel.** By Emil Abderhalden, Direktor des physiolog. Inst. der Univ. Halle A. S. 3 Aufl. Pp. 736—7¼ × 4½; M 21 brosch., M 23 gebund. Urban und Schwarzenberg, Berlin, Wien, 1914.

This well known Lehrbuch, which is indispensable in the biochem. laboratory, is no longer confined to one vol., but in its 3d ed. it appears in more than one. Lectures 1-13 of the 2d ed. (carbohydrates, lipins and proteins) have been rewritten and extended to 31 in the 3d ed. There are two additional new lectures (32-33), on hemoglobin, chlorophyll and their derivatives. This amplification has permitted the author to treat his subjects more fully, of course, and to add the essentials of the newer findings in the field covered by the volume. The lectures in the new ed. maintain their high reputation for comprehensiveness, clearness, force and interest. Part II, *Die anorganischen Nahrungsstoffe*, will probably be issued in the spring of 1914. Gies.

**A manual of bacteriology for agricultural and general science students.** By Howard S. Reed, prof. of mycology and bacteriology in the Va. Polytech. Inst.; plant pathologist and bacteriologist in the Va. Agric. Exp. Station. Pp. 179—6¼ × 4; 1.25. Ginn and Co., Boston, 1914.

An unusually concise, complete and effective manual. Presents a general course in bacteriology of particular value in technical schools, especially to students of agriculture. Includes a strong section outlining study of important fermentations caused principally by fungi. The author's extended experience has enabled him to make the manual comprehensive and practical in high degree. Presents unpublished matter and many useful suggestions for biochemists. Gies.

**Industrial organic chemistry;** adapted for the use of manufacturers, chemists, and all interested in the utilization of organic materials in the industrial arts. 4th ed. By Samuel P. Sadtler, consulting chemist, prof. of chemistry in the Phila. Coll. of Pharmacy, former prof. of organic and indust. chemistry in the Univ. of Penn. Pp. 601—7¼ × 4½; \$5.00 net. J. P. Lippincott Co., Phila., 1912.

The general plan of this standard volume remains unchanged, but a thoro revision has been made. The space devoted to analytical processes has been increased, bibliographies have been brought up to date and statistical matter wisely adjusted to the needs of the specialist. Occupying a position, in scope, between the exhaustive special treatises and ordinary hand-books, this volume is particularly useful to biochemists working on the border between pure and applied organic chemistry. The chapters of special biochemical interest are those on the industries pertaining to fats and fatty oils, essential oils and resins, cane sugar, starch and its alteration products, fermentation, wine, distilled liquors, bread, vinegar, milk, textile fibres of vegetable and animal origin, animal

## Books received (con.)

tissues and their products, dyes and dyeing. For the biochemist the book is unusually valuable as a work of reference. Gies.

**Chemische Apparatur;** Zeitschrift für die maschinellen und apparativen Hilfsmittel der chemischen Technik. Herausg., Dr. A. J. Kieser, Leipzig. I Jahrg., Heft 1, Jan. 10, 1914. Pp. 16—10¾ × 8; M 4.80 vierteljährh. Otto Spamer, Leipzig.

**The New York Journal of Pharmacy.** Prof. Curt P. Wimmer, man. ed. Vol. I, No. 1, Jan., 1914. Pp. 32—7¼ × 5¼; \$1.00 per year. Published monthly by the Alumni Assoc. of the N. Y. Coll. of Pharmacy, of Columbia Univ.

**Untersuchungen über Chlorophyll: Methoden und Ergebnisse.** By Richard Willstätter and Arthur Stoll, Kaiser Wilhelm Inst. für Chemie. Pp. 424—7¼ × 4¼; M. 20.50. Julius Springer, Berlin, 1913.

This comprehensive volume presents unpublished data, obtained by Willstätter and his pupils in recent years, on the isolation and hydrolysis of chlorophyll and the separation and quantitative determination of its component radicals. A complete compilation and revision of the essential data of Willstätter's classical studies on chlorophyll is included, and the relationship of chlorophyll and hematin is further clarified. The volume is encyclopedic in scope and presents the methods so clearly that it may be used as a laboratory handbook on chlorophyll. That it will aid and stimulate research on chlorophyll is certain and should be studied by biochemists generally. The volume is beautifully illustrated with eleven plates, which indicate details of the crystalline and spectral characters of the products. The work on which the book is based was a monumental achievement. (*See page 220 of this issue.*) Gies.

**The elements of the science of nutrition.** By Graham Lusk, prof. of physiology, Cornell Univ. Med. Col. Second ed. Pp. 402—6½ × 3¾; \$3.00 net. W. B. Saunders Co., Phila., 1909.

This widely appreciated volume, by a master of the subject in both its theoretical and practical phases, is one of the best on nutrition. We use it freely in our advanced courses, and await impatiently the appearance of the third edition. Gies.

**Nutritional physiology.** By Percy G. Stiles, assist. prof. of physiology, Simmons Col.; instr. in physiology and personal hygiene, Mass. Inst. of Tech., Boston. Pp. 271—6 × 3½; \$1.25 net. W. B. Saunders Co., Phila., 1912.

An admirable treatment of nutrition, which is very appropriately dedicated to the author's teacher, Prof. Graham Lusk. The chemical phases of physiology are concisely though none the less effectively considered; and nutrition is presented from the *dynamic* point of view without confusion with food chemistry. A very valuable addition to the growing supply of textbooks in biological chemistry for beginners. Gies.

**Essentials of pathological chemistry, including description of the chemical methods employed in medical diagnosis.** By Victor C. Myers and Morris S. Fine, prof. and instr. in path. chemistry, respectively, at the N. Y. Post-Grad. Med. Sch. and Hosp. Reprinted from the *Post-Graduate*, 1912-13. Pp. 137—7 × 4; \$1.25. Post Graduate (Med. Jour.), N. Y. City, 1913.

A very useful compilation of laboratory methods in the pathological chemistry of digestion and excretion, also of milk and blood, with an appendix of laboratory suggestions. The discussions are practical in guidance and broad in interpretation. The book is a very handy laboratory manual. We hope the authors will carry it through numerous revisions and extensions, as the science advances and methods multiply. Gies.

Books received (con.)

**Modern research in organic chemistry.** By F. G. Pope. Pp. 324—6 × 3½; \$2.25 net. D. Van Nostrand Co., New York, 1913.

Restricted, with interesting historical introduction, to chapters successively on polymethylenes; terpenes and camphors; uric acid (purin) group; alkaloids; relation between color and constitution of chemical compounds; salt formation, pseudo-acids and bases; pyrones; ketens, ozonides, triphenylmethyl; and the Grignard reaction. Masterly treatment of each subject. Constitutional formulas used freely and effectively. Gies.

**An introduction to the chemistry of plant products.** By Paul Haas (lecturer on chemistry, Royal Gardens, Kew) and T. G. Hill (reader in vegetable physiology, Univ. of London). Pp. 401—4 × 7; \$2.25 net. Longmans, Green and Co., 1913.

Excellent discussion of the chemistry and biological significance of many of the most important plant constituents. Besides extended treatment of carbohydrates, lipins and proteins, chapters are devoted respectively to glucosides, tannins, pigments, nitrogenous bases (alkaloids, ptomaines, purins), colloids and enzymes. Methods of preparation, detection and quantitative determination are numerous and well described. Good *subject* index. The most valuable recent contribution of its kind to phyto-chemistry. Strongly recommended to biological chemists generally—to botanists in particular. Gies.

**Practical physiological chemistry.** By Sidney W. Cole, demonstrator of physiology, Trinity College, Cambridge. Third edition. Pp. 230—4 × 6½; 7s. 6d. net. W. Heffer & Sons, Ltd., Cambridge, Eng., 1913.

Very useful laboratory manual. Subject treated chiefly from static point of view. Practical throughout. Methods well selected. Quantitative procedures given satisfactory attention. Special emphasis laid upon Folin's micro-chemical methods of urinary analysis. Good index. See review by Walter Jones, *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 1064. Gies.

**Reagenzien-Verzeichnis enthaltend die gebräuchlichen Reagenzien und Reaktionen, geordnet nach Autorennamen.** Dritte Aufl. By E. Merck. Pp. 446—8¾ × 5½. Julius Springer, Berlin, 1913.

Very useful in a biochemical laboratory. References to original literature with description of each reagent or test. Arrangement favors easy reference to desired author, substance or procedure. Gies.

**Annual report of the Virginia Polytech. Inst. Agric. Expt. Station for 1911 and 1912.** 1913 (13 original papers).

**Studies from the department of physiology, Cornell Univ. Med. Col., II.** 1913. (12 reprints.)

**Sloane Hospital for Women (N. Y. City): Obstetrical and gynecological reports.** Vol. I, 1913. Edited by Wilbur Ward. 1913.

**Radium: A monthly journal devoted to the chemistry, physics and therapeutics of radium and other radioactive substances.** Vol. I began with issue in April, 1913. Radium Publishing Co., Pittsburgh, Pa.

**Researches in biochemistry conducted in the Johnston Laboratory, Univ. of Liverpool.** Edited by Benjamin Moore, Johnston prof. of biochem., and Owen T. Williams, demonstrator of biochem. Vol. II; 1908-1911. (27 reprints.)

**Glycosuria and allied conditions.** By P. J. Cammidge. Pp. 467—4 × 6¾; \$4.50 net. Longmans, Green & Co., New York; Edward Arnold, London, 1913.

**The chemical constitution of the proteins: Part II, Synthesis, etc.** 2d ed. (One of the *Monographs on Biochemistry*.) By R. H. A. Plimmer, Univ. reader and ass't prof. of physiological chem., University Coll., London. Pp. 107—4¾ × 7½; \$1.20 net. Longmans, Green & Co., 1913.

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The BIOCHEMICAL BULLETIN is a quarterly biochemical review. It publishes results of original investigations in biological chemistry, preliminary reports of investigations, abstracts of papers, addresses, lectures, criticism, reviews, descriptions of new substances, methods and apparatus, practical suggestions, biographical notes, historical summaries, bibliographies, quotations, questions, news items, proceedings of societies, personalia, views on current events in chemical biology, and miscellaneous items of personal and professional interest to chemical biologists.

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### Future issues of the Biochemical Bulletin

Pursuant to a change of plan, which is referred to editorially on page 524, the first issue of Volume IV of the BIOCHEMICAL BULLETIN will be the January number. Hereafter, each volume of the BIOCHEMICAL BULLETIN will coincide, in periodicity, with the calendar years, instead of the academic years as heretofore. The new plan will enable us to issue the quarterly numbers promptly—in January, April, July and October.

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The members of the Columbia University Biochemical Association will coöperate confidentially with any one who desires the services of biological chemists or who seeks a position in biological chemistry.

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*Gust Kroneder.*

# BIOCHEMICAL BULLETIN

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VOLUME III

APRIL AND JULY, 1914

NOS. 11 AND 12

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## PROFESSOR HUGO KRONECKER

Hugo Kronecker, for the last thirty years professor of physiology at the University of Berne, Switzerland, died June 6. Although 75 years old, death surprised him in the midst of scientific activity. He attended the last meeting of the German Congress of Physiologists at Berlin where, on June 5th, he demonstrated experiments which should support the neurogenic theory of the origin of the heart beat. On his way home he stopped at Nauheim, to inspect an apparatus which he installed there for the study of and use in cardiac diseases. His death came there, suddenly, like a flash—perhaps by means of the cardiac center which he discovered thirty years before.

Kronecker was one of the last of a classical period in German physiology. He was pupil, assistant and intimate friend of the master minds of that period: Helmholtz, du Bois-Reymond and Carl Ludwig. At the same time, he was master and friend of many leading physiologists of a later generation and of many countries; he was an international leader in his science.

He was born in Liegnitz, Prussia, from a well-to-do family with scientific proclivities. The celebrated mathematician Leopold Kronecker was his older brother. After finishing his general education at the Gymnasium in Liegnitz he studied medicine in Berlin, Heidelberg and Pisa (Italy). In Heidelberg he came under the special influence of Helmholtz, who introduced Kronecker into the science of physiology. The problem of muscular fatigue, which Kronecker studied first under Helmholtz and which he treated in his thesis, became the source of many important investigations, which he carried out at various times during his scientific career.

In 1865 he became assistant to Traube. This celebrated clini-



cian was the first man to employ experimental physiology for the study of medical problems. It was probably due to the early influence of Traube that Kronecker acquired the inclination to make results, obtained in physiological studies, available for clinical medicine. On account of a temporary pulmonary affection, Traube sent him to Italy where he stayed for some time, an incident which left a mark upon Kronecker's future activities. The acquisition of the knowledge and use of the Italian language was unquestionably a factor in his future intimate relations with the Italian physiologists. He recovered his health and even served in the Prussian wars with Austria and France. In the Franco-Prussian war he received the iron cross for bravery.

1868 he entered Ludwig's celebrated "*Physiologische Anstalt zu Leipzig*" where he remained until 1876, becoming assistant in 1871, and Professor *extraordinarius* in 1874. In 1877 he was called to Berlin to become the Head of the division of experimental physiology in the Institute of Physiology, which had been recently organized by du Bois-Reymond. In 1884 he was called to Berne, where he filled the chair of physiology until the last day of his life.

Kronecker's scientific activities extended over more than half a century; his thesis appeared in 1863. But the investigation which raised him to the rank of a first-class physiologist was his work on "fatigue and recovery of striated muscles," published from Ludwig's Laboratory in 1872. The careful planning of the experiments, the exactness and skill with which they were executed, and the sharp analysis which permitted the derivation of general laws, put a classical stamp upon this piece of work; its celebrated tracings were the starting point for many future ergographic studies. The later work during his Leipzig period was mainly devoted to the cardiac muscle; some of the results found a permanent place in physiology. I may mention here the development of the "all and none" law; the loss of irritability of the cardiac muscle during systole (refractory period, Marey); the importance of inorganic salts for the heart beat (with Merunowitz and others).

Of his many investigations during his Berlin period I should mention the studies which led up to the use of transfusion as a life-saving means (present-day writers do not seem to know that Kron-

ecker was the inventor of this method); the extensive studies (with his collaborators) on the physiology of deglutition; the discovery of a coördinating center in the heart. I wish to record here the fact that Kronecker had an essential share in the development of the clinically important methods of studying blood pressure in human beings. The first human sphygmomanometric studies are usually ascribed to Von Basch, but Von Basch carried out these studies in Kronecker's laboratory and under his direction and assistance. I can testify to that as an eye-witness.

During his long stay in Berne a great many physiological subjects were investigated in conjunction with advanced co-workers or students. The results were usually published under the name of the co-workers. In the last years of his life he was intensely interested in experiments which could throw light upon the origin of the heart beat; he was a firm believer in the neurogenic theory.

A subject in which he took a great interest in the last two decades of his life was the nature and origin of mountain disease. The Swiss government, before granting permission to build the now famous Jungfrau railroad, asked Kronecker to pass an opinion, whether going up a high mountain in a railway would be accompanied by mountain disease and other disturbances of health. This gave rise to numerous studies connected with this question, Kronecker organized a party of sixty, who ascended the Zermat Breithorn; some of the party were carried up, in order to eliminate muscular action. Circulation, respiration and other functions were then investigated. The problem was also studied in pneumatic chambers with lowered atmospheric pressure. Kronecker came to the conclusion that the syndrome of mountain disease was primarily due to mechanical causes—to a stasis in the intrapulmonary veins brought about by rarification of the air in higher altitudes. Kronecker's publications gave rise to many international studies which caused the Italian physiologist Mosso, with the aid of Kronecker, to establish an international institute on Monte Rosa for the study of physiological phenomena in the mountains.

Kronecker was a master in physiological methods. He invented many instruments which found a permanent place in the methods of experimental physiology of which I shall mention here only his

well-known induction coil, divided into units; the "perfusion canula"; and the frog-heart manometer. The perfusion canula (or its modification) has been and still is extensively used in pharmacological studies upon the frog heart.

In the seventies, during Kronecker's stay at Leipzig, Ludwig's physiological institute was an international center for physiology and physiologists. Many English, Italian, American, Russian, Belgian, Scandinavian and French physiologists received there their training in physiology. Kronecker, who spoke many languages fluently, was of great assistance to them. With his very kind, unselfish nature he was always ready to help them with his rare experimental skill and in every other direction. Many who worked there during that period bear witness that Kronecker was the "soul" of the laboratory. Here he formed strong bonds of life long friendships with men who became, later, international leaders in science. I need only mention here Bowditch and Minot of the United States; Lauder Brunton, Gaskell and Schäfer of England; Alberto Mosso and Luciani of Italy; Paul Heger of Belgium and Holmgren of Sweden. Very few men had the happiness of having so many true friends as Kronecker, and few could be a truer friend than he. He had the esteem and affection of all who had the good fortune to know him well.

His international, cordial relations to so many physiologists of so many countries was not a small factor in the success of the International Congress of Physiologists, which was founded by Michael Foster and Kronecker. In his obituary of Sir Michael Foster, Gaskell states that "when the International Medical Congress met in London in 1881 he (Foster) and Kronecker together drew up a scheme for a separate International Congress of Physiology to meet every three years and a committee was formed." According to Heger the final decision, to call that Congress into being, was made by a group of physiologists who met, September 1888, in Kronecker's house in Berne. The third International Congress met in Berne under Kronecker's presidency.

Kronecker was also the chief founder, and for some time the president, of the Institut Marey in Paris, an international institution for the study of physiology by the newest and most approved methods.

The Hallerianum, Kronecker's magnificent physiological laboratory in Berne, has been for years an international center for physiological investigators. English, American, Italian and Russian students went there to learn methods and to be initiated in physiological research. Well-known physiologists often worked in this laboratory: for instance, Cyon, Gamgee, Heger, and others. At his attractive home, presided over gracefully by Mrs. Kronecker, a cultured lady and an accomplished linguist, one often met celebrated scientists from all over the world. Kühne, Mosso, Bowditch, Schäfer and Foster were often there.

Kronecker was a foreign member of our National Academy of Sciences, of the Royal Society and of many European Academies. He had conferred upon him honorary degrees from a great many Universities. In England alone he received the degree of LL.D. from the Universities of Glasgow, Aberdeen, St. Andrews and Edinburgh, and the degree of D.Sc. from Cambridge.

He had pupils all over the world. Of American investigators who worked under Kronecker at one time or another I shall mention only the following: Mills, Stanley Hall, Cushing, Gies, H. C. Jackson, H. C. Wood, Jr., Cutter, Carter, Busch, Mühlberg, Mays, McGuire, Arnold and Meltzer.

Before concluding I wish to call attention to the following few incidents which bear witness to the nobility of Kronecker's character. The phenomenon of the "refractory period," which is generally ascribed to Marey, was observed and clearly described by Kronecker one year before Marey. Kronecker never made any effort for the recognition of his priority, and both physiologists remained intimate friends during their entire lives. I have mentioned above that Kronecker had a share, at least equal to that of Von Basch, in being one of the first who introduced the era of studying blood pressure in human beings. But when Von Basch and others neglected to give him credit, we find Kronecker nowhere making an effort to obtain his rights.

Kronecker's studies of the nature of mountain disease was a stimulus which gave rise to researches on that subject by many other investigators, among whom I shall mention Zuntz and Loewy and A. Mosso, who came to results differing from those of Kron-

ecker. It was, however, in Kronecker's laboratory that Loewy made the analyses of his results; and I have been a witness of the attractive scene when Mosso was introduced by Kronecker to his students to lecture on Mosso's theory of acapnia as the cause of mountain disease, a theory entirely at variance with his own.

Kronecker had many scientific disputes, and was often energetic and perseverant in the defense of his views. But he never permitted a personal note to slip into his discussions.

Physiology lost in Kronecker a master and a leader, and numerous physiologists all over the world lost in him a noble and kind-hearted friend.

S. J. MELTZER.

*Rockefeller Institute,  
New York*



## THE VISCOSITY OF BILE

R. BURTON-OPITZ

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Guided largely by the supposition that the viscosity of a fluid bears a direct relationship to its viscous resistance, it has generally been assumed that the viscosity of bile is very great. Moreover, as the composition of bile differs widely in different groups of animals and varies considerably even in the same species, it has been conjectured that its viscosity is subject to equally pronounced variations. Both of these assumptions, however, are not substantiated, because, as will be shown later, the viscosity of bile does not necessarily suggest its viscous resistance and neither is it permissible to estimate the latter solely with the aid of data pertaining to its composition.

In attempting to procure exact values for the viscosity of bile I have made use of the procedure previously employed by me in determining the inner friction of various types of shed blood.<sup>1</sup> A glass capillary the dimensions of which have been accurately measured, is placed in a horizontal position in a long metal box filled with water. The lumen of the capillary-tube communicates, on the one hand, with a small tubular receptacle containing the bile to be tested and, on the other, with the receiving cups of the "switch". The free end of the receptacle is connected in turn with a pressure bottle and with a mercurial manometer. The temperature of the surrounding water must be kept constant by placing a small flame underneath the metal box. The bile is permitted to flow through the tube during a definite period of time which is accurately recorded by means of tambours and a chronograph.

This arrangement permits of the determination of the exact quantity of bile which is forced through the capillary-tube in a given time and under a certain pressure. When taken in conjunction with

<sup>1</sup> Burton-Opitz: *Pflüger's Archiv*, 1900, lxxxii, p. 464.

the specific gravity, and the length and diameter of the capillary, these factors enable the experimenter to calculate the coefficient of the viscosity. Moreover, in order that the latter convey a clear meaning to the reader, it may be compared with the coefficient of the viscosity of distilled water heated to 37° C. which possesses the numerical value 4700. The viscosity of bile, as well as that of any other fluid, may therefore be expressed in terms of multiples of this coefficient.

The present determinations have been made with ox bile obtained from the animals at slaughter by incising the gall-bladder, as well as with bile collected in the same manner from dogs during ether narcosis.<sup>2</sup> As the amount procured from a single animal was generally very small, the specific gravity was tested with the aid of pycnometers containing 5 c.c. and less of fluid. The diameter of the capillary measured 0.41 mm.; its length, 29.0 cm. These tests were made at a temperature of 37° C.

Table I proves first of all that ox bile possesses a viscous resistance which is very much slighter than that of dog bile. The coefficients here found vary between 2260 and 2718, and show the average value of 2511; and hence, ox bile presents a viscosity which is only 1.8 times greater than that of distilled water at 37° C. Moreover, when compared with the coefficient for the circulating blood of the dog, which is 950, it is seen that this body-fluid possesses a viscous resistance only about one-third as great as that of blood.<sup>3</sup> This result agrees perfectly with the values for the specific gravity, which vary between 1.0178 and 1.0207, and also with the fact that ox bile contains only traces of mucin.

The experiments with dog bile have given values ranging between 541 and 1074, and the average coefficient 723. Clearly, therefore, this fluid possesses a viscosity which is much above that of ox-bile and, in a slight measure, also above that of ordinary blood. Compared with distilled water at 37° C., it exhibits a viscous resistance 6.5 times greater and equal to that of a "thick" type of blood.

<sup>2</sup> On account of rather stringent laws intended to govern the performance of autopsies, I have not been able to gather very satisfactory data regarding normal human bile. It seems best, therefore, to postpone the publication of these data until a later date.

<sup>3</sup> Burton-Opitz: *Pflüger's Archiv*, 1900, lxxxvi, p. 406.

In accordance with the high viscosity, the specific gravity shows in these cases variations between 1.0355 and 1.0459. While it is quite evident that dog bile possesses also a greater viscosity than ox bile, it cannot be conjectured that its high viscosity is directly dependent upon its content in mucin or similar substances. To be sure, these two qualities of the bile generally preserve a direct relationship to one another, but examples may also be cited which clearly show that a high viscosity is at times associated with a low viscosity, and

TABLE I  
*Data pertaining to viscosity of bile*

	Number of experiment	Number of determ.	Spec. gravity	Quantity mg.	Time sec.	Pressure mm. Hg	Viscosity coefficient	Average for each exp.	Greatest difference	Average for each group
Ox Bile	1 {	1	1.0207	476.0	19.17	109.1	2288.5	2260.5	457.8	2511.7
		2	—	766.0	33.30	103.6	2232.6			
	2 {	1	1.0189	405.3	24.84	60.7	2707.6	2718.3		
		2	—	511.5	32.78	57.6	2729.0			
	3 {	1	1.0205	329.9	27.51	48.2	2502.1	2521.5		
		2	—	330.7	30.09	43.5	2540.9			
	4 {	1	1.0178	896.6	29.49	121.4	2525.3	2546.5		
		2	—	726.3	24.50	120.4	2482.9			
Dog Bile	1 {	1	1.0400	514.9	44.43	172.4	663.40	665.8	532.2	723.8
		2	—	462.2	40.27	169.5	668.24			
	2 {	1	1.0459	390.2	25.71	217.7	684.05	686.9		
		2	—	451.6	30.46	210.9	689.82			
	3 {	1	1.0445	357.5	33.65	169.9	614.42	610.5		
		2	—	264.3	25.45	168.2	606.67			
	4 {	1	1.0436	355.7	28.76	161.6	752.68	764.2		
		2	—	344.6	27.35	159.7	775.91			
	5 {	1	1.0455	198.1	32.70	111.9	531.45	541.8		
		2	—	142.3	25.07	100.9	552.21			
	6 {	1	1.0355	415.2	29.74	130.0	1064.5	1074.0		
		2	—	353.1	26.11	123.7	1083.6			

vice versa. In illustration of this statement, I mention the results obtained with bile collected from a patient who had suffered for some time previously from a severe inflammation of the gall-bladder

and biliary passages. This condition having been relieved by an operation, the patient continued to discharge large quantities of an extremely viscid bile. But, in spite of the fact that the bile collected in surprisingly heavy strings when poured from the beaker, it traversed the capillary-tube with greatest ease. The coefficient of the viscosity showed the numerical value 2218 and, hence, this type of bile was only 2.1 times more viscous than distilled water at 37° C. Its specific gravity was very low, namely 1.010.

Just the reverse relationship between these two factors was found to exist in bile which I procured at autopsy from a person who had suffered from septic pericarditis and lobar pneumonia. The liver was enlarged and markedly hyperaemic. In spite of the fact that this bile exhibited no unusual degree of viscosity, its viscosity was very high, namely, 9.8 times greater than that of distilled water at 37° C. Its specific gravity was high, namely 1.039.

#### THE EFFECT OF CHANGES IN TEMPERATURE UPON THE VISCOSITY OF OX BILE

It has been shown that the viscous resistance of dog bile is already very considerable at a temperature of 37° C. On subjecting it to lower temperatures, its viscosity increased steadily until, at 20° C., several of the samples enumerated in Table 1 became so viscous that they could scarcely be forced through the capillary tube. Thus, one sample which, at 37° C., had shown a viscosity 7.0 times greater than that of distilled water, became 15.8 times more viscous at 20° C.

The three experiments enumerated in Table 2 have been made with different samples of ox bile. Beginning at 20° C., two determinations were made at 30° and 37° C. in each case. A glance at the column containing the average values, clearly proves that the viscosity decreases very markedly with increasing temperature. Thus, if Experiment 2 is selected for illustration, it is seen that the coefficient 1766.9 obtained at 20° C. is changed to 2359.1 at 30° C. and to 2718.3 at 37° C. Compared with distilled water, the initial ratio of 1:2.6 becomes 1:2.0 at 30° C. and 1:1.7 at 37° C. It is also evident that the change in the viscosity is not constant for each degree of temperature, but becomes steadily slighter as the high

TABLE 2

*Data pertaining to the effects of changes in temperature upon viscosity of bile*

	Tem- perature °C.	Number of deter- mina- tion	Specific gravity	Quantity mg.	Time sec.	Pressure mm. Hg	Vis- cosity coeff- icient	Average values	Differences
Exp. 1.....	20 {	1	1.0262	893.3	29.93	187.2	1594.7	1597.2	469.6
		2	—	825.4	27.91	184.9	1599.8		
	30 {	1	1.0230	556.9	14.67	184.1	2068.8	2066.8	193.7
		2	—	530.9	14.09	183.0	2064.7		
	37 {	1	1.0207	476.0	19.17	109.1	2288.5	2260.5	
		2	—	766.0	33.30	103.6	2232.6		
Exp. 2.....	20 {	1	1.0227	648.4	22.62	163.7	1757.5	1766.9	592.2
		2	—	540.3	20.85	146.4	1776.4		
	30 {	1	1.0201	493.6	25.02	84.1	2360.1	2359.1	359.2
		2	—	540.7	28.48	81.0	2358.0		
	37 {	1	1.0189	405.3	24.84	60.7	2707.6	2718.3	
		2	—	511.5	32.78	57.6	2729.0		
Exp. 3.....	20 {	1	1.0245	394.1	22.65	109.1	1597.9	1620.6	604.0
		2	—	393.8	23.98	100.1	1643.4		
	30 {	1	1.0222	403.2	28.08	65.5	2201.1	2224.6	296.9
		2	—	356.6	26.94	61.7	2154.1		
	37 {	1	1.0205	329.9	27.51	48.2	2502.1	2521.5	
		2	—	330.7	30.09	43.5	2540.9		

TABLE 3

*Data pertaining to changes in the viscosity of ox-bile on standing*

		Number of determination	Specific gravity	Quantity mg.	Time sec.	Pressure mm. Hg	Viscosity coefficients	Average values	Greatest difference
Exp. 1....	Normal.... {	1	1.0189	405.3	24.84	60.7	2707.6	2718.3	120.3
		2	—	511.5	32.78	57.6	2729.0		
	On standing {	3	1.0180	465.6	20.14	82.9	2811.7	2838.6	
		4	—	586.2	27.83	77.0	2757.9		
Exp. 2....	Normal.... {	1	1.0205	329.9	27.51	48.2	2502.1	2521.5	123.2
		2	—	330.7	30.09	43.5	2540.9		
	On standing {	3	1.0196	566.6	29.66	72.7	2644.9	2644.7	
		4	—	455.5	24.52	70.7	2644.6		



temperature limit is approached. If projected as a curve, the values here obtained would therefore give rise to a curved line, conforming thereby in general to water and watery solutions. The decrease in the viscosity is associated with equally pronounced reductions in the specific gravity.

When permitted to stand for a time at room temperature, ox bile undergoes certain autolytic changes which, as the experiments compiled in Table 3 will show, also affect the viscosity. The two samples of bile here tested gave the coefficients 2718 and 2521, or if compared with distilled water at 37° C., the ratios 1:1.7 and 1:1.8 respectively. Four days later the same samples showed the values 2838 and 2644, or the ratios 1:1.6 and 1:1.7. A slight decrease in the viscosity has therefore taken place during this time, which is associated with an inconsiderable decrease in the specific gravity.

# NOTES ON THE TOXICITY OF DILUTE SOLUTIONS OF CERTAIN PHENOLIC COMPOUNDS AS INDICATED BY THEIR EFFECT ON AMPHIBIAN EGGS AND EMBRYOS, TOGETHER WITH REFERENCES ON MODIFICATIONS OF PIGMENT DEVELOPMENT

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## I. INTRODUCTION

We believe it to be a fairly well established fact that the black melanic pigment results from the interaction of an oxidizing enzyme of the tyrosinase type and some oxidizable chromogen, the exact nature of which has never been elucidated [Gortner, 1911 (a)]. One of us [Gortner, 1911 (b)] has shown that *m*-di-hydroxy phenols inhibit the action of tyrosinase *in vitro* and the suggestion was made that perhaps certain types of colorless animals owe their lack of pigment to the presence of inhibitory compounds.

During the last two years we have been testing the effect of dilute solutions of certain organic compounds upon pigment development in amphibian larvae. A preliminary note as to the effect of some of these solutions upon pigmentation has already appeared [Banta-Gortner, 1913 (a)], but inasmuch as the place of publication is not readily accessible to the chemist, a brief statement of some of the results has been incorporated in this paper together with the data relating to the toxicity of these compounds. The observations on toxicity were incidental to the investigations on pigmentation (to be published in detail in a biological journal) and, although fragmentary, they are perhaps of sufficient value to record.

<sup>1</sup> This paper represents coöperative effort, each author having as nearly as possible an equal share in the work.

## II. EXPERIMENTAL

EXPERIMENTS WITH "TRIKRESOL" (COMMERCIAL). Eggs of the wood frog (*Rana sylvatica*) and of the salamander (*Amblystoma punctatum*), in early stages of development, were killed in less than 24 hr. when placed in a trikresol sol. stronger than 0.05 percent. The eggs in 0.05 percent sol. were dead in 72 hr., without any sign of further development after having been placed in the sol. The eggs in 0.01 percent sol. were all alive at the end of 96 hr. and had developed almost as well as the control eggs, but they then gradually died. At the end of a week all of the eggs with the exception of two salamander eggs were dead. These live eggs were at the blastopore stage while the check eggs were in the neural groove. No further development occurred. When a sol. of 0.005 percent conc. was used, all frog eggs were dead at 7 days, while the salamander eggs were only slightly retarded. The development of the salamander embryos continued but slightly behind the control material for 41 days, at which time the larvae had been hatched for a week. These larvae were normal but somewhat smaller than those in the control.

When eggs of the salamander, *Spelerpes bilineatus*, were tested it was found that the retardation of development was much the same as for *Amblystoma*. *Spelerpes* eggs lived in 0.01 percent trikresol for 14 days, at which time they showed traces of pigment. The control series was at this time deeply pigmented.

EXPERIMENTS WITH 3-5-DI-HYDROXY TOLUENE (ORCINOL). Orcinol inhibits the action of tyrosinase upon tyrosin *in vitro* and we hoped to be able to inhibit, or at least to modify the course of, pigment development by rearing larvae in sol. of orcinol. Considerable work was done with eggs and embryos of the frogs, *Rana sylvatica* and *Hyla pickeringii*, the salamander, *Amblystoma punctatum*, and other amphibian eggs and larvae, before it was noted that the exposure of orcinol sol. to light caused a great increase in its toxicity. As a result all of the eggs and larvae were very soon killed. When, however, the sol. is kept in a dimly lighted room, and when fresh sol. is placed on the eggs at least three times a week, it is possible in large measure to diminish the toxicity.

The only materials which we have studied on a large scale, since

noting the increased toxicity of the sol. due to the action of light, are the eggs and embryos of *Spelerpes bilineatus*. This salamander egg is without pigment, so that the early development of pigment in the embryo can be easily followed. A total of about 150 experiments were run on this material using conc. of 0.0125–0.025 percent. We obtained in every instance a retardation of growth, accompanied by a much greater retardation in pigment development, than would correspond to the retardation in growth. In some of the experiments, where the conc. of orcinol was low and the time of immersion was short, we did not obtain permanent after-effects and the later course of development resembled that of the control. When, however, the strength of the orcinol was high (0.02–0.025 percent) and the treatment sufficiently prolonged, varying from 1 day to a week or more depending on the initial age of the embryo, we have apparently obtained permanent modifications. The nature of these effects depends somewhat on the initial age of the egg or embryo. When eggs at a stage of development between the early blastula and the late neural groove are kept in the sol. less than 6 days, they rarely show types as abnormal as those which have been exposed to the action of the drug for from 6 to 20 days. They do show, however, the typical retardation of pigment development and various other characteristics sufficient to classify them as "modified."

When these early embryos are kept in the sol. for more than 6 days, the course of development is much different. The larva develops in many cases normally, although somewhat slowly, until within a short time before hatching when huge swellings appear, sometimes filling the entire body with great serous cavities through the walls of which may be seen the alimentary canal and the blood vessels, stretched almost to breaking. In this condition they may live for some days but eventually die without further development.

If, however, the embryos are older when first treated, *i. e.*, with the head strongly differentiated or at any later stage up to the beginning of pigmentation (which occurs shortly before hatching), the effect is widely different. In no instance do we obtain the blistered larvae but instead short, heavy individuals, about one third shorter and twice as broad as the controls. These we class as the true "orcinol type." They are distinguished from the controls by

their shorter length, greater girth, absence of any conspicuous spots, development of heavy awkward "flippers" in place of delicate limbs and toes, coarse reticulation of the pigment pattern, sluggish movements and disability, or disinclination, to take food. This last trait prevents our knowing how permanent this type may be, for they gradually grow smaller and eventually die of starvation in an average of 8-9 weeks after hatching.

It would thus appear that, although orcinol is very toxic in excess of 0.025 percent conc., it is not nearly so toxic as is some other substance [oxidation product (?)] formed by the action of light on an orcinol solution. The formation of this new compound can be easily observed by the development of a pink color, deepening to red as the reaction progresses. In solutions of 0.025 percent or weaker the toxic effect, although still marked, is of much less interest than the remarkable influence which the drug exerts upon the course of development. Sol. of 0.005 per cent conc. showed but little toxic effect when kept in a dimly lighted room and had little or no effect upon the course of development.

EXPERIMENTS WITH *m*-DI-HYDROXY BENZENE (RESORCINOL). A total of 150 experiments were made using eggs and embryos of *Spelerpes bilineatus*. As with orcinol, we found that resorcinol is much less toxic when the sol. is kept in the dark than when exposed to the light. A very dilute sol. of resorcinol (0.005 percent) becomes very toxic when placed for a time in bright light, the sol. deepening in color from colorless to light yellow to brownish orange.

We find that resorcinol is more toxic than orcinol, but that both have a similar influence on the course of development, the "resorcinol type", however, being perhaps still more definite than the corresponding "orcinol type." The same swellings are produced when young embryos are placed in sol. of the drug. When eggs are treated before reaching the blastula, no larvae are hatched.

Perhaps the most noteworthy feature of the resorcinol experiments is that dealing with the inhibition of pigmentation. When larvae are treated with resorcinol sol. (0.02-0.05 percent) after the head is well differentiated, up to within a day or two of the beginning of pigmentation, and are kept in the sol. a sufficient length of



time (4-10, or more, days depending on the initial age of the embryo), a considerable retardation in development is produced as well as a great retardation of pigment production. The first pigment appears in the eye to be followed, a little later, by a narrow "V" on the shoulders and, a day or two later, by a narrow line down the spine. This condition persists so long as the larvae remain in the resorcinol sol., but the toxicity of the drug is so great that even in so low a conc. as 0.0125 percent, death ensues after an immersion of 15-18 days even when the sol. is changed daily. In many instances we have had larvae in resorcinol sol. which were almost entirely devoid of pigment, excepting for their eyes, when the control animals (from the same group of eggs) were fully pigmented and had the entire larval pigment pattern fully developed.

When the larvae are removed from the sol. after varying lengths of time, depending on the initial age of the embryo, we obtain two distinct types of animals. The more extreme type resembles the orcinol type but is heavier, the flippers are more enlarged, the pigment reticulations are ~~fine~~ as contrasted with the coarse reticulation of the orcinol type. This type persists for 60-70 days when kept in water, but since the animals do not feed, death by starvation eventually ensues.

The second type probably represents individuals which have not been so profoundly modified. The body form is practically normal, but the typical pigment pattern does not develop, the pigmentation being very fine and dull in color. The majority of this type also die of starvation. In nearly every instance, in both the orcinol and resorcinol series, the larvae remain, until death, much lighter in color than those individuals in the control series.

The greater number of the experiments, where eggs and embryos of *Rana sylvatica*, *Hyla pickeringii*, or *Amblystoma punctatum* were used, were carried out before we had noted the extreme toxicity produced by the action of light on resorcinol sol., and are therefore only records of very rapid deaths. Inasmuch as all of these eggs contain pigment, the differences in pigment development could not be easily followed.

The eggs of *Rana sylvatica* and *Amblystoma punctatum*, when treated in the early developmental stages, produce in the larvae the

extreme edema noted in the *Spelerpes* larvae. It is not unusual to observe serous cavities almost large enough to hold the entire body of a normal larva. The normal increase in size of the embryo is, to a large extent, brought about by the imbibition of water, and it would seem that dilute sol. of orcinol or resorcinol may so influence this process as to destroy the delicate balance of the mechanism which regulates the amount of water absorbed; as a result the water flows through the epidermis until the tension produced by the tightly stretched body wall prevents any further osmosis. If these phenols in such small conc. can produce such a result, it seems possible that edemic conditions may be traced, in other instances, to a similar action by minute traces of poisonous metabolic products retained within the tissues.

EXPERIMENTS WITH *p*-DI-HYDROXY BENZENE (HYDROQUINONE). Developing eggs and embryos of *Spelerpes bilineatus*, *Rana sylvatica*, *Hyla pickeringii* and *Amblystoma punctatum*, when placed in sol. of hydroquinone of 0.25–0.005 percent conc., were dead in every instance within 24 hr. The dilution was not carried lower than 0.005 percent.

EXPERIMENTS WITH *o*-DI-HYDROXY BENZENE (PYROCATECHIN). Developing eggs of the amphibia noted above were placed in sol. of pyrocatechin of 0.5–0.005 percent conc. All the frog eggs were dead within 24 hr.; the jelly was darkened, varying from deep smoky to black depending on the conc. of the pyrocatechin. The eggs of *Spelerpes* were also all dead within 24 hr. in all dilutions, the colorless egg having become brownish in color and the egg membranes a bluish black. The eggs of *Amblystoma* were apparently much more hardy; those in conc. of 0.05 percent or greater died within a few hours, but in 0.01–0.005 percent conc., they continued to live for several days, although their development was very greatly retarded and never passed the blastopore stage. The membranes in all cases assumed a deep smoky color.<sup>2</sup>

<sup>2</sup> In collaboration with Dr. Goodale one of us (G.) injected hen eggs with various chemicals to determine effects upon the course of development. One of these chemicals was pyrocatechin—about 1 c.c. of 1 per cent. sol. to each egg. In every case the eggs were found soon to show an intense opacity when candled and, upon opening them, the contents were found to be almost as black as ink. This is probably the result of an oxidation, possibly induced by an oxidizing enzyme, but tyrosinase is absent from the hen egg, or at least gives no corresponding color

EXPERIMENTS WITH 1-2-3-TRI-HYDROXY BENZENE (PYROGALLOL). Pyrogallol in a conc. of 0.005 percent or greater caused the death of all amphibian eggs tested within 24 hr. The sol. assumed a brown color, its depth depending on the conc. of the drug. The eggs were also stained a brownish tint.

EXPERIMENTS WITH 1-3-5-TRI-HYDROXY BENZENE (PHLOROGLUCINOL). Phloroglucinol is readily acted on by light when in sol., the colorless sol. becoming a brownish orange. This orange sol. is intensely toxic. From the position of the hydroxyl groups we expected to find that phloroglucinol had a toxicity as great or greater than that of resorcinol. In a series of 20 experiments with *Spelerpes* eggs and larvae and in a large number of tests using eggs and embryos of both frogs and other salamanders, we have found, however, that, if the sol. is not exposed to the action of light, the toxicity of a sol. of a conc. as great as 0.05 percent., and, in the few instances tested, of as great a conc. as 0.5 percent, is almost negligible. In conc. of 0.025 per cent, on the contrary, there is a slight acceleration of pigmentation and probably of general development, indicating a stimulating instead of a toxic effect. Even *Daphnia*, which is unusually sensitive to an unfavorable medium, seem to live well in this conc. of phloroglucinol.

EXPERIMENTS WITH  $\alpha$ - AND  $\beta$ -NAPHTHOL,  $\alpha$ - AND  $\beta$ -NAPHTHYLAMINE, *p*-AMINO PHENOL, *p*-PHENYLENEDIAMINE, DI-AMINO PHENOL (AMINO GROUPS?), AND MONO-METHYL-*p*-AMINO-*m*-CRESOL. The behavior of these compounds is so similar that they may be classed together. The first four compounds, when used in conc. of 0.005 percent or greater, kill developing eggs within a few hours. With  $\alpha$ -naphthol and  $\alpha$ -naphthylamine the membranes of *Amblystoma* eggs are stained a deep magenta. The other compounds were tested in only one conc., *i. e.*, 0.1 percent; they all caused the death of the eggs in a very short time. It may be of interest to note that while many of these compounds possess great toxicity in as low a conc. as 50 parts per million (0.005 per cent), a saturated sol. of di-hydroxy stearic acid [which has just this conc. and which Schreiner and Skinner (1910) have shown to be decidedly injurious to wheat seed- with tyrosin sol. The blackening of the jell of the *Rana sylvatica* eggs can be easily explained by the presence of large amounts of tyrosinase [Banta-Gortner, 1913 (b)].

lings] is without any noticeable effect upon either the embryos or larvae of *Spelerpes* or *Amblystoma*.

EXPERIMENTS WITH TANNIN (COMMERCIAL). Tannin inhibits oxidase action and it was hoped that low conc. of tannin might prove less toxic than either orcinol or resorcinol, and still inhibit the formation of pigment. We have found, however, that tannin in as low a conc. as 0.0125 percent kills *Spelerpes* eggs and embryos within 24 hr. The dead eggs are more or less swollen, depending on the conc. of the tannin sol. used; and when eggs in cleavage stages were used, the cells of the dead eggs were sharply outlined by being pulled apart from each other. This is probably an edemic condition.

EXPERIMENTS WITH PYROCATECHIN MONO-METHYL ESTER (GUAIACOL). Sol. of guaiacol of 0.1-0.005 percent conc. were tested on developing eggs of *Rana sylvatica*, *Amblystoma punctatum*, and *Spelerpes bilineatus*. The higher conc. killed the eggs within a very few hr. Using sol. of 0.005 percent conc., all of the different species of eggs developed slowly for 10-15 days, but eventually died before hatching. The toxic effect is best observed by the extreme retardation of development. In conc. of 0.025 per cent or greater the inner membrane of the *Amblystoma* eggs is colored a bright pink.

EXPERIMENTS WITH *p*-HYDROXY-PHENYL- $\alpha$ -AMINO PROPIONIC ACID (TYROSIN). Mathews (1909) and King (1912) have tested the effect of a saturated sol. of tyrosin on developing eggs of *Arbacia* and *Chaetopterus*. They found that tyrosin caused a marked retardation of development but that no specific abnormalities were produced. In weaker sol. than saturation, Mathews observed in some cases a slight acceleration of the general development, but in most cases either no change from the normal or a slight retardation. Tyrosin is so slightly soluble (1 part in 2454 parts of water) that a high conc. cannot be tested. In a saturated sol. we have noted an apparent toxicity, but this is at most only slight. It seems possible that a large part of this toxicity may be due to the presence of bacteria in the sol., for tyrosin sol. seemed to be very favorable for the growth of bacteria. In some instances jars containing eggs and tyrosin sol. have become infected with bacteria to such a degree



that the liquid was almost solidified and poured like a thin jelly. In such a sol. the larvae remain suspended, being unable to swim. Such an infection may result within 1-2 days. In other instances the tyrosin sol. becomes a bright pink and later deposits black humin. In such instances the bacterial infection probably secreted tyrosinase. No effort has been made to identify any of the bacteria concerned in these phenomena. We feel, therefore, some hesitancy in ascribing any definite toxic properties to tyrosin itself, although in a saturated sol. it may show some slight toxicity to the eggs which we have used. In like manner our results regarding the question of pigmentation are not as satisfactory as we could wish. A number of our experiments gave results that were not different from those for the control material, while a few of the experiments produced animals with less pigment, and developing less rapidly, than the control. We have come to regard the negative outcome of these experiments as arising from bacterial infection.

The work on tyrosin embraced series of all of the amphibian eggs with which we have worked in other experiments. Since the course of pigmentation can be followed best in the larvae of *Spelerpes*, and since no noteworthy results aside from pigmentation have developed, we shall confine our details to the experiments involving *Spelerpes*.

There were 41 experiments with *Spelerpes* in tyrosin sol., each experiment involving many embryos. Twenty experiments showed no effect of the treatment; 11 of these 20 had been subjected to a conc. of less than 0.008 percent and most of the remaining 9 experiments had been influenced by the bacterial infections or had at first shown some effect of the treatment and had later "reverted."

Twenty-one experiments, comprising 220 individuals, were profoundly influenced by the treatment and became "good" or "typical" tyrosin types. The tyrosin influence is shown by (1) the more rapid appearance of pigment in the individuals in tyrosin sol. as contrasted with the controls; (2) the extremely small size and later the entire absence of pigmentless spots in the larvae, the areas where spots are normally visible being filled with dense black pigment;<sup>3</sup> and (3) the dense dull black color of the larvae compared

<sup>3</sup> From this observation it would seem probable that the pigment pattern, at least in so far as it relates to the presence of spots without the melanin, is formed



with which the control animals often appear comparatively light. There is no mistaking the "tyrosin type," for an inexperienced person will always pick them out as the darkest individuals in a series.

EXPERIMENTS WITH *p*-HYDROXY-PHENYL ETHANOL (TYROSOL). Tyrosol was prepared from tyrosin by the action of yeast (Ehrlich, 1911). When treated with tyrosinase it was found that the typical black color could not be obtained, only the soluble colors of the system, tyrosin-tyrosinase, being produced, *i. e.*, pink to rose to red. Inasmuch as tyrosol differs from tyrosin only by an amino and a carboxyl group attached to the  $\alpha$ -carbon atom of the aliphatic chain, it seems probable that the soluble colors produced by the action of tyrosinase on tyrosin are the result of a quinone formation acting on the *p*-hydroxyl group, and that the production of the black humin involves the aliphatic amino group.

Since tyrosol is acted on by tyrosinase to produce a red color, we thought the color of the larvae of *Spelerpes* might be influenced by rearing them in sol. of tyrosol. Conc. of tyrosol varying from 0.1-0.0125 percent were employed. The higher conc., 0.1-0.05 percent, proved to be quite toxic, causing the death of the larvae within 15 days. The retardation of growth was very marked as was also the retardation of pigmentation. Whether there was a greater retardation of pigment development than could be explained by the retardation in growth and general body development we are unwilling to state without the aid of larger series of material. Those animals which were placed in sol. of tyrosol of 0.025-0.0125 percent conc., showed retardation in general body development and slowness in the development of the normal pigment pattern. However, after about a month in the sol., they reached a stage where they were "indistinguishable from the controls" and shortly after this time they were discarded.

by a localized secretion of the chromogen while the oxidizing enzyme is distributed through the skin tissues of the entire body surface. Such a hypothesis will serve to explain the absence of spots in the larvae treated with tyrosin, which would take the place of the chromogen. From the previous work of one of us [Gortner, 1911 (c)], it seems probable that this is the case in the development of the color pattern of *Leptinotarsa decemlineata*.

## III. SUMMARY OF GENERAL CONCLUSIONS

1. Amphibian eggs and embryos are killed by a 0.05 percent sol. of "*trikresol*" within 72 hr. A sol. of 0.01 percent conc. kills wood frog embryos within a few days but salamander eggs withstand this amount of the drug for some time, although the development is much retarded.

2. *Orcinol*, in 0.05-0.01 percent conc., is fairly toxic. Young amphibian embryos are killed within 10-12 days, while older embryos may withstand 14-18 days treatment. Treatment for 6 days or more produces retardation in growth, and a considerable inhibition in pigment development. With the longer or stronger treatments, especially with the younger embryos, very abnormal types are produced, many of which are edemic. Certain oxidation (?) products of orcinol, produced by the action of light, have many times the toxicity of orcinol.

3. *Resorcinol* is slightly more toxic than orcinol. It has a similar effect upon the course of development. With the material used it is more effective than orcinol as an inhibitor of pigmentation. While, in general, resorcinol produces the same types of abnormalities, they are more extreme and occur in a larger percentage of cases than with orcinol.

4. *Pyrocatechin*, *pyrogallol*,  $\alpha$ - and  $\beta$ -*naphthol*,  $\alpha$ - and  $\beta$ -*naphthylamine*, in conc. of 0.005 per cent, killed all frog and *Spelerpes* embryos within 24 hr. In this conc. of pyrocatechin, *Amblystoma* embryos developed very slowly and died within a few days. A solution of di-hydroxy stearic acid of this conc. is without noticeable effect upon *Spelerpes* or *Amblystoma*.

5. *Phloroglucinol* is doubtfully toxic in dilute (0.05 per cent) sol. When acted on by light the sol. becomes very toxic.

6. *Tannin* kills all amphibian eggs within 24 hr. in conc. of 0.0125 percent.

7. *Guaiacol*, in conc. greater than 0.005 percent, kills within a few hours. A sol. of 0.005 percent conc. greatly retards development and kills within 15 days.

8. *Tyrosin* is, at most, only slightly toxic at saturation (0.04 percent). Bacterial infections are very common and make the sol. fairly toxic so as sometimes to slightly retard development and occa-

sionally to reduce pigmentation. In most cases a marked *increase* in pigmentation occurred when the embryos were kept in sol. of tyrosin of 0.01-0.04 percent conc. during and after the onset of pigmentation.

9. *Tyrosol*, in conc. as great as 0.05 percent, retarded growth and pigmentation, and killed *Spelerpes* larvae within 15 days. Weaker sol. retarded growth and pigmentation but did not prove fatal, and in time the animals developed the usual amount of pigment.

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## THE DIGESTIBILITY OF MAIZE CONSUMED BY SWINE

Brief preliminary report on work done coöperatively by the  
Chemical and Animal Husbandry Sections of the Iowa  
Agricultural Experiment Station.

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Maize, the most abundant of our fat and energy producing cereals, being the grain in greatest demand for meat production, has been the subject of numerous interesting and practical experiments, especially in connection with swine. The Iowa Station has conducted feeding trials to compare the value, in the production of pork, of whole corn on cob, shelled corn and ground corn, the two latter being fed both dry and soaked.

For further comparison of the manner in which swine utilize maize fed in these forms, digestion trials were conducted with heavy-weight hogs, about twelve months old and 200 lb. in weight; also with light-weight swine, approximately 80 days old and weighing about 70 lb. The comparative digestibility of maize fed in five forms to swine of different age and weight, was thus studied.

The apparent digestibility was determined by weighing and analyzing the feed and corresponding feces, the latter being collected in rubber bags which were held in place on the animals by means of a specially constructed harness. In preparation for analysis, all moist samples were treated with formalin and air-dried.

Experiments have been conducted in three different years: the first, in the summer of 1909, with ten heavy-weight hogs; the second, in the summer of 1910, with the same number of light-weight animals; the third, in the fall of 1911, with as many of both light- and heavy-weights.

With both classes of swine each year, two different lots of five animals each were subjected to a digestion trial extending through

two ten-day periods, during which they were kept in cages, each animal receiving throughout the periods one kind of grain, viz., whole grain on the cob, dry or soaked shelled, or dry or soaked ground grain. The feces produced from the feed eaten during the ten days was distinguished by a charcoal marker given at the beginning and end of each period.

The averages of results obtained in all the experiments thus far conducted are given for light and heavy animals respectively, in the accompanying table:

TABLE I (A-B)

*A. Data pertaining to average digestibility of maize eaten by light-weight swine*

Feed	Digestion coefficients of the food constituents						
Method of preparation	Dry matter	Protein	Nitrogen-free extract	Crude fiber	Ether extract	Ash	Organic matter minus ether extract
Whole grain, on cob . . . . .	88.86	78.18	93.59	43.80	72.42	20.50	89.96
Shelled grain, dry . . . . .	88.05	76.00	93.16	45.42	73.85	7.36	89.39
Shelled grain, soaked . . . . .	87.20	76.24	92.78	45.17	62.87	7.32	88.74
Ground grain, dry . . . . .	87.22	76.60	92.88	42.00	59.40	10.92	88.82
Ground grain, soaked . . . . .	85.91	70.50	92.11	38.92	67.91	— 5.29	87.68

*B. Data pertaining to average digestibility of maize eaten by heavy-weight swine*

Whole grain, on cob . . . . .	85.42	74.79	90.67	19.65	66.85	24.85	86.33
Shelled grain, dry . . . . .	86.48	74.39	91.56	43.46	64.22	23.88	87.45
Shelled grain, soaked . . . . .	85.40	74.51	90.66	40.85	58.18	15.98	86.40
Ground grain, dry . . . . .	87.25	73.14	92.65	39.72	65.03	20.64	88.33
Ground grain, soaked . . . . .	88.39	77.13	93.37	39.40	59.57	18.05	89.27

Taking dry matter as a basis for comparison, the tables indicate that the light-weight swine digested whole grain on cob, and shelled grain more thoroughly than did the heavy swine, while the latter utilized the soaked ground grain to better advantage than the former. The light swine have the highest digestion coefficient for whole grain on cob, then dry shelled, dry ground, soaked shelled and soaked ground grain, respectively, whereas with the heavy-weights the soaked ground grain has the highest digestibility, then, successively, dry ground, dry shelled, ear, and soaked shelled corn.

The figures in Table I are in close agreement with those obtained



in similar experiments, at the Ohio Station,<sup>1</sup> by Dr. Forbes, who has very kindly shown us some of his results. Dr. Forbes took into consideration metabolic nitrogen, however, which was not done in this work.

A remarkable correlation between digestibility and time required for digestion was found in the series of experiments conducted in 1909-10; it was brought to notice by observations on the interval between the ingestion of bone black and its appearance in the feces. This correlation may be seen in Table 2, which shows the average length of time required for charcoal to traverse the digestive tract.

TABLE 2

*Data pertaining to average time required for charcoal to traverse the digestive tract of swine*

Comparison of rate of alimentary movement and digestibility						
Feed	Light-weights, 1910			Heavy-weights, 1909		
	Hours	Digestion coefficients. Dry matter	Number of observations	Hours	Digestion coefficients. Dry matter	Number of observations
Whole grain, on cob...	70.5	90.96	7	38	86.29	6
Whole grain, dry.....	54.0	88.80	8	48	87.04	6
Whole grain, soaked...	48.0	88.09	8	36	84.97	6
Ground grain, dry.....	57.0	88.40	8	36	86.46	6
Ground grain, soaked..	40.5	84.52	8	50	88.61	6

More time was required for the food to pass through the alimentary canal of the light-weight swine in every case, except the soaked ground grain, than was required for this process by the heavy-weights. The former also digested all the preparations, excepting soaked ground grain, more thoroughly than did the latter. The same kind of correlation exists to some degree for each class of swine. Thus, with the younger swine, the ear corn was most digestible, then dry shelled, dry ground, soaked shelled and soaked ground in the order mentioned. The ear corn remained longest in the digestive tract, then dry ground, dry shelled, soaked shelled, and soaked ground grain, respectively.

The older swine digested soaked ground maize the most advan-

<sup>1</sup> Ohio Agric. Exp. Station, *Bulletin* No. 271; published since the above was written.

tageously, then dry shelled, dry ground, ear, and soaked shelled grain, successively. The soaked ground corn required the longest time for traversing the alimentary tract, then dry shelled, ear, dry ground and soaked shelled, the latter two being equal in this respect.

The above correlation between digestibility and the time during which the feed remains in the alimentary canal, does not appear in the results obtained from the 1911 series of experiments; therefore, more investigation is needed along this line.

The results obtained in our digestion trials agree fairly well, in a general way, with feeding experiments which have demonstrated that light hogs, weighing less than 200 lb., make the most rapid gains with whole corn on cob, in the natural state; while heavy-weight swine make the most rapid gains with the soaked shelled and soaked ground grain. Discrepancies in results of the different experiments are explained to a great extent by the necessarily small number of swine used in the digestion trials, while in the feeding experiments many more animals were examined, thus eliminating the factor of individuality.

## EXPERIENCE WITH THE ABDERHALDEN SERUM TEST FOR PREGNANCY.

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An enormous literature has already developed since Abderhalden's publication relative to the serum diagnosis of pregnancy. Many have doubted the value of the test while others have found it of great virtue and reliability. Shortly after Abderhalden's description of the test I began to use it. I have been uniformly successful in its application, and am firmly convinced of its reliability for the diagnosis or elimination of pregnancy.

In applying the test I have followed Abderhalden's directions minutely and have always set up three tests for each serum, viz., serum alone, placenta alone and serum with placenta; and, of late, I have also included a positive control and a negative control.<sup>1</sup> This is advisable on account of the fact that serum alone will often give a positive reaction, especially if the serum is obtained at any time within 8 hours after the last previous meal. For that reason I examine, at present, only sera obtained in the morning before breakfast.

In the summary on the succeeding page, I have tabulated certain of my results with this test, which show its reliability and value. In tests 39-50, the recorded positive or negative results were verified, at later dates, by the appearance or non-appearance of absolute signs of pregnancy, or by operation; the positive results were found to be coincident with pregnancy.

In this work I have used the dialysis method entirely, and both the biuret and ninhydrin tests were applied to the dialysate in each case.

<sup>1</sup> Full descriptions of the technic may be found in Abderhalden's *Abwehrfermente des tierischen Organismus* (1913), and in Webster's *Diagnostic methods* (1914, p. 613.)

*Data pertaining to results with the "Abderhalden serum test" for pregnancy.*

No.	Clinical diagnosis.	Result of Abderhalden test.	No.	Clinical diagnosis.	Result of Abderhalden test.
1	Normal male	O	28	5-Month pregnancy	+
2	Normal male	O	29	4-Month pregnancy	+
3	Normal male	O	30	3-Month pregnancy	+
4	Normal male	O	31	3-Month pregnancy	+
5	Normal male	O	32	2-Month pregnancy	+
6	Normal male	O	33	2-Month pregnancy	+
7	Normal male	O	34	2-Month pregnancy	+
8	Normal male	O	35	7-Month pregnancy	+
9	Female child	O	36	7-Month pregnancy	+
10	Female child	O	37	2 weeks after delivery	+
11	Female child	O	38	2 days after delivery	+
12	Female child	O	39	Neurotic vomiting	
13	Female child	O		or pregnancy	O
14	Female child	O	40	Neurotic vomiting	
15	Non-pregnant adult	O		or pregnancy	O
16	Non-pregnant adult	O	41	Neurotic vomiting	
17	Non-pregnant adult	O		or pregnancy	+
18	Non-pregnant adult	O	42	Neurotic vomiting	
19	Non-pregnant adult	O		or pregnancy	+
20	Non-pregnant adult	O	43	Ectopic or appendicitis	O
21	Non-pregnant adult	O	44	Ectopic or appendicitis	O
22	Non-pregnant adult	O	45	Ectopic or appendicitis	+
23	Non-pregnant adult	O	46	Myoma or pregnancy	+
24	Non-pregnant adult	O	47	Myoma or pregnancy	+
25	Non-pregnant adult	O	48	Myoma or pregnancy	+
26	8-Month pregnancy	+	49	Myoma or pregnancy	O
27	8-Month pregnancy	+	50	Myoma or pregnancy	O

## A NOTE ON THE USE OF PURIFIED ANTIGEN OF BESREDKA IN THE SERUM DIAGNOSIS OF TUBERCULOSIS

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In a preliminary communication before the Society for Experimental Biology and Medicine, last February,<sup>1</sup> one of us reported results of a series of experiments in the serum diagnosis of tuberculosis with Besredka's tuberculin as antigen. The stated conclusions were that, although this reaction seemed to be specific in tuberculosis, yet the fact that the antigen contains lipin (derived from culture media on which the tubercle bacillus is grown), opens the possibility that certain non-tuberculous sera having lipotropic properties might fix the complement with this antigen. In order to avoid this possible non-specific reaction it was proposed to delipinize the antigen.<sup>2</sup>

In a large series of experiments, in which the tuberculin of Besredka was deprived of its lipins by means of extraction with ether in a separatory funnel, it was found that the antigenic properties of this tuberculin were not injured thereby.<sup>3</sup> It was also found that, in spite of the fact that a comparatively large number of syphilitic sera fixed the complement in presence of Besredka's tuberculin, this fixation was not due to the presence of lipin in the tuberculin, but to the fact that apparently these syphilitics, either on account of their disease or because of the antisyphilitic treatment, are highly susceptible to tubercular infection.

<sup>1</sup> Bronfenbrenner: *Proc. Soc. Exp. Biol. Med.*, 1914, xi, p. 92.

<sup>2</sup> We use "delipinize" rather than "delipolize" (formerly employed by us), in order to avoid suggestions of lytic effects. "Delipinize" depends upon and accords with the convenient use of the term "lipins" to designate *fats and lipoids collectively*. See Wells: *Chemical Pathology*, 1914, p. 23.

<sup>3</sup> These findings have been confirmed lately by Renaux: *Compt. rend. soc. biol.*, 1914, lxxvi, p. 864.



Having thus proved that the lipin fraction of the tuberculin has no antigenic value in the complement deviation test of tuberculosis, and therefore can be removed and thus the antigen purified, we sought to determine further what fraction, if any, of the protein part of the tuberculin is responsible for its antigenic properties. Tuberculin contains protein materials from egg-white and egg-yolk, also proteose, peptone, amino acids and other soluble protein derivatives in the beef broth, as well as different products resulting from the cleavage of said substances in the nutrition of tubercle bacilli. The problem of isolating each protein and protein derivative, and testing for any corresponding antigenic values, therefore, is a very difficult one, but we are endeavoring to study it following the suggestions of Professor Gies.

## THE DIAGNOSTIC VALUE OF THE LANDAU TEST FOR SYPHILIS

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The specificity originally attributed to the Wassermann reaction, in the sense that this reaction depends on the combination between antibody in blood of the syphilitic individual with its specific antigen derived from syphilitic liver extract, is no longer tenable, since it was shown that not only syphilitic liver but normal liver, or any other organ of human as well as animal origin, yields substances that are capable in combination with syphilitic serum to inactivate or fix the complement. The extreme sensitiveness of the reagents that have to be continuously titrated adds to the complexity of this test. Although not specific in the original sense the Wassermann reaction is, however, a fairly constant finding in syphilis, and in this sense its specificity is very well established.

Landau<sup>1</sup> has lately described a chemical test which is not only very much simpler than the Wassermann reaction but, according to Landau, is also more specific. The test is based on the property of syphilitic serum (or possibly of the nonsaturated fatty acids contained in it) to combine with iodine. In a series of 90 cases of syphilis he found the Wassermann reaction positive 49 times whereas the Landau reaction was positive 55 times. In his later publication Landau changed slightly the technic of this test and, by doing so, markedly facilitated the reading of the results. In a series of 77 cases of syphilis, tested by the improved method, the positive results obtained by Landau were 27 percent higher than those obtained by Wassermann reaction. Judging from Landau's results the test offers a very valuable addition to the laboratory methods now in use. We therefore planned to repeat his work, and to compare the results obtained by his reaction with those obtained by the Wassermann reaction, as the latter is used in our laboratory.

<sup>1</sup> Landau: *Wien. klin. Woch.*, 1913, p. 1702.

Inasmuch as Landau suggested that each worker establish the optimum conditions for the test, and since he calls attention to the lability of the active principle in the syphilitic serum, we made a series of preliminary experiments, to develop a uniform technic for all the cases of our series. From the very beginning it was quite apparent that certain sera give a positive reaction, that others give a negative reaction; and when examinations are duplicated, the results of multiple examinations of the same sera invariably agree. It is clear that certain sera possess a definite capacity to combine with iodine and, in doing so, to form compounds which do not respond to the starch test for iodine.

Our preliminary experiments have shown, however, that almost all sera possess this property to a greater or less degree; and, if left for a longer time, many negative sera, not having combined with iodine at first, fix it ultimately. In his original article Landau suggested that the test be allowed to stand for 5-15 hr. before reading. Our preliminary experiments have shown, however, that this indefinite technic may lead to very confusing results, for some sera give very definite positive reactions even at the end of 1 hr. after the addition of iodine mixture, some only after 3-5 hr., some only after 10 hr., and others only after 24 hr. Comparatively few sera fail to combine with iodine by the end of 24 hr. In view of these facts we permitted the mixtures to stand long enough to allow all the sera giving a positive Wassermann reaction to combine with iodine and found, in doing so, that 16 hr. was the best time limit.

Another important question to decide was the uniform age of the serum, as Landau in his publication warned against the use of old sera on account of their tendency to lose affinity for iodine. From our experiments in this connection it became apparent that although some sera retain their property to fix iodine unchanged, for even as long as 48 hr., other sera seem to undergo, on standing, certain changes that cause them to lose or to acquire the property to fix iodine. We therefore adopted the uniform use of sera obtained 6 hr. after collection of the blood.<sup>2</sup>

Having thus eliminated the uncertain points in the technic of the test, we proceeded to examine a series of 220 cases, using the follow-

<sup>2</sup> We also found that heating the sera for 30 min. at 56° C., did not change their properties in reference to fixation of iodine.

ing uniform procedure: 25 mg. of pure metallic iodine were emulsified in paraffin oil; 2.5 cc. of this liquid were mixed with 0.2 cc. of the fresh (6 hr.) serum to be tested. The mixture was shaken in a small test tube closed with a cork stopper, then placed in the dark for 16 hr., when 2 drops of starch sol. were added to the contents of each tube. The normal sera gave a dark blue coloration, whereas the syphilitic sera remained colorless or were colored slightly blue.<sup>3</sup>

*Data pertaining to the Wassermann and Landau tests*

		W.+ L.+	W.+ L.—	W.— L.—	W.— L.+	Total number		
						W. +	L. +	Cases
Syphilis treated and untreated	Number of cases	78	21	31	20	99	98	150
	Average.....	52%	14%	21%	13%	66%	65%	—
Normal controls	Number of cases	0	0	49	21	0	21	70
	Average.....	—	—	70%	30%	0	30%	—

As may be seen from the accompanying summary, we succeeded in bringing the total number of positive Landau reactions in the cases of known syphilis up to 65 percent, which equals the percentage of positive Wassermann reactions in the same cases, but in doing so we obtained also 30 percent of positive Landau reactions among the normal controls.

Without attempting to discuss the results, it is clear that the Landau reaction is not more specific than the Wassermann reaction. Although in 20 cases of syphilis, where the Wassermann reaction was negative, the Landau was positive (which at first would suggest a greater sensitiveness of the Landau reaction over the Wassermann); in 21 other cases the results were the opposite, as can be seen from the table. On the other hand, out of 70 cases in which no syphilis was diagnosed (where there was no indication of this disease in the patient's history and where Wassermann reaction was invariably negative), 21 cases gave a positive Landau reaction,—a fact that definitely speaks against its specificity.

<sup>3</sup> In 100 cases out of the 220 we also used the modified technic of Landau, namely, the iodine was completely dissolved in carbon tetrachloride in the proportion of 50 mg. of iodine to 5 c.c. of carbon tetrachloride. For each 0.2 c.c. of serum 0.1 c.c. of this iodine solution was added. Syphilitic sera, after 4 hr. at room temperature, remain transparent and show a yellow reddish color, whereas normal sera become grayish white and opaque. In general we failed to find this technic any better than the first described.

The latter observation is confirmed also by the recent report of Kissmeyer,<sup>4</sup> who found the Landau reaction positive in 51 percent of his normal control cases.

Although the findings reported above speak against specificity for the Landau reaction (at least in its present form), it is very interesting to recall that not all sera have equal power to fix iodine. Moreover, although fixation occurs also with sera of nonsyphilitics (30 percent), the frequency of fixation of iodine among syphilitics is much greater (65 percent). The problem is a very interesting one.

On the basis of our experience we wish to call attention to at least two very important factors in this connection which make a study of this problem very difficult: One is the importance of establishing the duration-time of the test, in order to avoid a too low (in case of short duration) or a too high (in case of long duration) percentage of positive reactions. Another important difficulty is the lack of an objective standard with which to compare the results, since the results of the Wassermann reaction are far from being uniform in the hands of various workers.

The nature of this interesting phenomenon observed by Landau is an object of further study in our laboratory.

<sup>4</sup> Kissmeyer: *Hospitaltid*, 1914; cited from *Deutsche med. Woch.*, 1914, p. 927.



## FURTHER STUDIES ON BESREDKA TUBERCULIN

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Since the first publication by Besredka and Manoukhine,<sup>1</sup> on the use of the new tuberculin of Besredka for the serum-diagnosis of tuberculosis, several authors, using in some cases a technic differing from the original, have reported very favorable results with this tuberculin as antigen in the complement-deviation test. Besredka and Manoukhine, though expressing their confidence that their method was of diagnostic value in tuberculosis, noticed from the beginning that certain syphilitic sera had a tendency to fix complement in presence of this tuberculin. They tried, therefore, to guard against possible error from this source by limiting the use of the reaction to cases in which syphilis could be excluded. Several investigators have confirmed both the specificity of the reaction in tuberculosis and the comparative frequency of positive findings in syphilis.

Early in the year one of us had the opportunity of reporting results<sup>2</sup> of some experiments with Besredka tuberculin. The conclusions reached were, that although the reaction seemed to be specific in tuberculosis, yet the fact that the antigen contained lipin derived from the medium on which the tubercle bacilli culture is grown, indicates a possibility that certain non-tuberculous sera having lipotropic properties, as for instance syphilitic sera, might fix the complement with this antigen. In order to avoid this possible non-specific reaction, it was proposed to delipinize the antigen. In a large series of experiments, in which the tuberculin of Besredka was deprived of lipins by means of extraction with ether, it was found that the antigenic properties of the tuberculin were not injured thereby.<sup>3</sup>

<sup>1</sup> Besredka and Manoukhine: *Compt. rend. soc. biol.*, 1914, lxxvi, p. 180.

<sup>2</sup> J. Bronfenbrenner: *Proc. Soc. Exp. Biol. Med.*, 1914, xi, p. 92.

<sup>3</sup> Similar findings have been reported since by Renaux: *Compt. rend. soc. biol.*, 1914, lxxvi, p. 865.

In another communication<sup>4</sup> it was pointed out that whenever the complement deviation with Besredka antigen is present in sera with high lipotropic properties, it depends on the presence of a separate tuberculous antibody possessing its own index different from the lipotropic index of the same serum. It was found, moreover, that the lipins which can be extracted from the tuberculin with ether, chloroform, benzene or petroleum-ether are not sufficient, in the quantity in which they are present in the tuberculin, to cause a fixation of the complement in presence of lipotropic sera.

Since the appearance of this publication, we have succeeded in isolating the active principle of the tuberculin by means of precipitation with ten volumes of absolute alcohol. Another efficient method was the precipitation of protein from the tuberculin by adding two drops of glacial acetic acid to 10 c.c. of Besredka tuberculin which produced a heavy precipitate. This precipitate, when centrifuged, suspended in 10 c.c. of physiological salt sol. and neutralized to phenolphthalein, proved to be an excellent antigen, practically free from any lipin except the small amount adherent to the precipitate.

It was noticed, however, that different samples of antigen received at different times from Professor Besredka's laboratory evidently differed as to their antigenic value. How wide the range of these differences in apparently similar samples of tuberculin was found to be, is shown by the data in Table 1.

Whatever may be the cause of the comparatively low percentage of positive reactions obtained, among cases of active tuberculosis, with the antigen IV, the fact that the percentage of positive reactions among syphilitics is so decidedly higher with it, suggested the necessity of a renewed study of the rôle of the lipin fraction of the tuberculin used in this series. The results of this study were the following: Whereas, with products I and II, the amount of lipin that could be extracted from the tuberculin by shaking with different solvents was found to be too small to cause non-specific lipotropic fixation; in the case of tuberculin IV, the amount of lipin thus obtained was not only sufficient to explain the high percentage of positive reactions with syphilitic sera, but was almost sufficient for use as antigen in the Wassermann reaction, as can be

<sup>4</sup> J. Bronfenbrenner: *Archives of Internal Medicine* (in press).

seen from the following: Tuberculin IV was precipitated with glacial acetic acid; the precipitate was extracted repeatedly with alcohol-ether mixture and the extract evaporated to dryness; the residue was taken up with 2 cc. of methyl alcohol and subsequently further diluted with physiological salt sol. to the volume of the tuberculin from which the lipins originated.

TABLE I  
*Data pertaining to differences among various preparations of Besredka tuberculin*

		Tuberculin I and II	Tuberculin IV
		Percentage of positive reactions	Percentage of positive reactions
No syphilis suspected. Tuberculosis diagnosed or suspected.	Active tuberculosis at present..	93.84	20
	Definite history of tuberculosis, but no symptoms at present. (Convalescents).....	55.5	0
	Tuberculosis strongly suspected, but not diagnosed definitely..	72	10.52
	Tuberculosis suspected or not suspected; also syphilis treated or untreated.....	37.96	64.7
No syphilis nor tuberculosis suspected.	Different pathological conditions, also surgical, obstetrical, gynecological cases, and cases without any history at the time of the serum test—accidents.....	8	1.9

This emulsion of lipins was then used as if it were syphilitic antigen in parallel series with a preparation of lipins originating from beef heart, which we are using for the routine diagnosis of syphilis. Both emulsions were tested in varying quantities against a constant amount of complement, amboceptor and known syphilitic serum (Table 2).

TABLE 2  
*Comparative data on lipin products from Besredka tuberculin as syphilitic antigens*

	0.1 cc.	0.07 cc.	0.05 cc.	0.03 cc.	0.02 cc.	0.01 cc.	0.007 cc.	0.005 cc.	0.003 cc.
Syphilitic antigen.....	+	+	+	+	+	+	<+	<<+	—
Lipins from Tuberculin IV.....	+	+	<+	.....	.....	.....	.....	.....	.....
Lipins from Tuberculin II.....	—	—	—	.....	.....	.....	.....	.....	.....

It was found that, when concentrated many times, the emulsion of lipins from tuberculin II was also able to fix the complement with syphilitic sera but, in the amount in which it was present in the tuberculin (Table 2), it was not sufficient to cause the non-specific fixation.

If we seek causes that account for the evident differences in apparently similar samples of Besredka tuberculin, several possible answers suggest themselves. (1) Since the tuberculin consists of the culture media in which tubercle bacilli have grown for a certain length of time (and there necessarily exist a number of possible variations affecting the rate of growth of different lots of cultures), different cultures are likely to contain variable amounts of the metabolic products of the organism. (2) A further source of variation lies in the fact that, in the process of preparation, tuberculin is heated under pressure to kill the tubercle bacilli and some unrecorded variations in the heating process might cause destruction of the antigenic value of the protein fraction of the tuberculin. (3) Moreover, it followed from our comparison of different tuberculins<sup>5</sup> used as antigens in the complement-deviation test, that in tuberculosis (as well as in other diseases), there exists a certain variability of specificity with different strains of tubercle bacilli, which probably necessitates in turn the preparation of a polyvalent antigen containing not only several human but also bovine strains. (4) The fact that the composition of Besredka tuberculins, in reference to the number of strains and respective amounts of each in given tuberculin preparations, might differ, would also account, possibly, for the observed variations in the antigenic value of the tuberculins. (5) Lastly, variations in the amounts of egg yolk, which is the primary source of the lipins in the antigen, probably affect the chemical qualities of the medium, of which the tuberculin is mainly composed.

Whatever the reasons for the differences may be, the very possibility of such variations suggested the necessity of standardizing the antigen in some way so as to insure uniform results with any

<sup>5</sup> We take this opportunity to thank most sincerely Prof. W. H. Park of the N. Y. Board of Health, as well as Dr. E. M. Houghton of Parke, Davis and Co., and Dr. A. P. Hitchens of Mulford Company, who kindly added different preparations of their tuberculins to our own series.

sample of the tuberculin. As this would mean an increase for some specimens, a decrease for others, in the concentration of the active principle in the tuberculin, we attempted to find what fraction of the bulk of the tuberculin was directly responsible for its antigenic properties.

We are obliged to Professor W. J. Gies for his valuable suggestions as to the methods to be employed for the study of this problem. Our work is temporarily interrupted on account of unforeseen conditions preventing us from getting new supplies of antigen from Professor Besredka, but will be continued as soon as possible.



## STUDIES ON SO-CALLED PROTECTIVE FERMENTS

### 1. The sensitization of substratum for the Abderhalden test.\*

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Recently the Bordet-Gengou discovery of the phenomenon of complement fixation stood at the center of interest in immunology; today, Abderhalden's discovery of the existence of specific ferments has taken its place. Probably both deal with the same set of questions and problems, but Abderhalden's theory substitutes for terms of immunology terms of chemistry, and designates, as specific ferments, the reactive complexes in the body juices which before were named anti- and immune-bodies. Although it is as yet too early to say what new ideas Abderhalden's theory has afforded for the understanding of the mechanism of chemical defense in the body, as compared with those formulated by Ehrlich, it is already possible to say that it has rendered a great service by giving a method for the detection of antibodies or defensive ferments where previous methods failed to distinguish them.

In 1909 one of us, while working in the laboratory of Professor Metchnikoff, attempted, at the suggestion of Dr. Weinberg, to search for specific antibody in the blood of pregnant animals, using placenta as antigen, but various attempts in this direction failed to bring about a satisfactory method of diagnosis of pregnancy. We have therefore lately attempted to determine whether the substances brought into play in the Abderhalden reaction are of the nature of antibody, as "antibody" was understood in 1909, or are entirely different.

Although we do not assert to have found definite proof that the nature of the defensive ferments is identical with that of the antibody or amboceptor, the results of our experiments seem, nevertheless, to contribute additional evidence to the effect that a certain amount of parallelism between the two undoubtedly exists.

\*The work described in this paper was inaugurated in March, 1914.

The first evidence pointing in this direction was offered by Abderhalden and his pupils, when they found that only fresh sera of pregnant women were capable of cleaving the placenta-protein in the Abderhalden reaction. The natural suspicion regarding the rôle of the complement in the test, led Stephan<sup>1</sup> to discover the fact (later confirmed by Hauptmann<sup>2</sup> and others) that the addition of fresh rabbit, guinea-pig, or any other, serum might reactivate inactive serum, and thus render the test possible with old sera.

In our own experiments we tried to make use of the known property of antibody of sensitizing the antigen at a low temperature, which excludes the activity of the complement. We found that there was not only no dialysis in the tube containing placenta and the pregnant serum when the temperature was low, but also that the placenta as well as the serum underwent changes absolutely similar to those we should have expected if we had used, instead, a hemolytic amboceptor and corresponding erythrocytes—namely, the serum was deprived of its property of digesting fresh placenta-protein, and the placenta-protein acquired the property of being digested by any fresh serum. Moreover, such a placenta (sensitized?) could also be digested by serum which was deprived of its specific antibody by exhaustion with placenta in the ice-box.

The accompanying summary gives the essentials of our results.

These findings are not only of theoretical importance, inasmuch as they furnish further proof of the similarity of the phenomenon of the Abderhalden to the immunity reaction, but are also of practical value. To those making routine examinations by the Abderhalden method, it is known that the blood of a patient taken under certain conditions, as when there is high temperature, pus formation, or recent ingestion of a meal, may contain an amount of amino acid sufficient to mask the specific reaction. Whereas the last mentioned factor can be regulated with little inconvenience to the patient, blood being taken before breakfast, it is impossible to obviate the complications in the other cases. In such instances, where the serum alone contains dialysable reactive substances, the difference in the strength of the reaction with ninhydrin of the control tube, and the tube containing placenta (or other substratum), as well as serum,

<sup>1</sup> Stephan: *Münch. med. Woch.*, 1914, no. 15, p. 801.

<sup>2</sup> Hauptmann: *Münch. med. Woch.*, 1914, no. 21, p. 1167.

furnishes the basis of diagnosis, but undoubtedly this may be a source of many errors. A modification was offered therefore by Schlimpert, which removes this source of error by subjecting the serum to dialysis prior to applications of the main test, using subsequently such serum deprived of its dialysable material for the digestion with placenta.<sup>3</sup>

Positive serum	Conditions	Normal control serum
Negative	1.5 c.c. of serum + substratum (on ice 18 hrs.). Ninhydrin test on dialysate.	Negative
Negative	The contents of respective thimbles were centrifuged and serum separated. Washed substratum <sup>4</sup> + water, 1.5 c.c. (in thimble at 37° C., 18 hrs.). Ninhydrin test on dialysate.	Negative
Positive	Washed substratum + fresh guinea-pig serum, 0.05 c.c. + water, 1.5 c.c. (37° C., 18 hrs.). Ninhydrin test on dialysate.	Negative
Negative	Washed substratum + heated guinea-pig serum, 0.1 c.c. + water, 1.5 c.c. (37° C., 18 hrs.). Ninhydrin test on dialysate.	Negative
Positive	Washed substratum + 1.5 c.c. of serum previously exhausted with substratum on ice (37° C., for 18 hrs.). Ninhydrin test on dialysate.	Negative
Negative	Serum separated from the substratum after exhaustion on ice 18 hrs., + fresh substratum at 37° C. for 18 hrs. Ninhydrin test on dialysate.	Negative
Negative	Serum separated from the substratum after exhaustion on ice 18 hrs., + fresh substratum + complement at 37° C. for 18 hrs. Ninhydrin test on dialysate.	Negative

Our own study suggests another possible modification of the procedure of the Abderhalden test, which would take advantage of the property of the substratum of being sensitized by a specific serum so as later to give up dialysable substances when put in contact with

<sup>3</sup> Schlimpert and Issel: *Münch. med. Woch.*, 1913, no. 32, p. 1758; also Abderhalden and Wildermuth: *Ibid.*, 1914, no. 16, p. 862.

<sup>4</sup> In all cases "washed substratum" stands for the substratum acted upon by the specific serum at low temperatures, centrifuged, separated from the serum, and washed in water.

any human or animal fresh serum, and would permit the examination of serum taken at any time, no matter what the condition of the patient might be. This modified procedure is the following: After remaining over night in contact with the suspected serum in the ice-box, the placenta (or other substratum, as the case may be) is centrifuged, washed with water to remove any serum that may stick to it, and placed in a new thimble with any serum that happens to be on hand. The best for this purpose is serum from a guinea-pig kept without food long enough (6-8 hours) to free its blood from dialysable reactive substances. It is necessary, of course, to take the additional precaution, in the diagnosis of pregnancy, of using male guinea-pig serum, since fresh serum from a pregnant guinea-pig gives a positive reaction with human placenta, and may thus cause grave error.

# EFFECT OF SALICYLIC ALDEHYDE ON PLANTS IN SOIL AND SOLUTION CULTURES

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(WITH PLATES 6-7)

The presence of salicylic aldehyde in some agricultural soils, together with the rather frequent appearance of aldehyde material in unproductive soils, as demonstrated by work in this laboratory,<sup>1</sup> has lent considerable interest to the study of the action of this compound on plants.

Salicylic aldehyde was accordingly tested in regard to its action on various plants in solution cultures and in soil in pots. The solution culture method comprised the growth of plants in water and in nutrient culture solutions. The method of procedure was essentially that described in previous publications.<sup>2</sup> The paraffined wire pot method was used in making the soil cultures.<sup>3</sup>

The action of the salicylic aldehyde is also being tested with crops in the field, and some of these results with cowpeas, garden peas and stringbeans are published elsewhere.<sup>4</sup> It was uniformly toxic.

## SOLUTION CULTURES

**EFFECT ON WHEAT.** Salicylic aldehyde was used in amounts of 10, 25, 50, 100 and 200 p.p.m.<sup>5</sup> dissolved in pure dist. water. A

<sup>1</sup> Shorey, E. C.: Some organic soil constituents, *Bul. 88, Bureau of Soils, U. S. Dep't Agri.* (1913); also, Schreiner, O. and Skinner, J. J. Occurrence of aldehyde in garden and field soils. *Jour. Franklin Inst.*, 178, 329 (1914).

<sup>2</sup> Schreiner, O., and Skinner, J. J.: Some effects of a harmful organic soil constituent, *Bul. 70, Bureau of Soils, U. S. Dep't Agri.* (1910).

<sup>3</sup> Gardner, F. D.: The wire-basket method for determining the manurial requirements of soils, *Cir. 18, Bureau of Soils, U. S. Dep't Agri.* (1905).

<sup>4</sup> Schreiner, O. and Skinner, J. J. Field tests with a toxic soil constituent: salicylic aldehyde. *Jour. Amer. Soc. Agron.*, 6, 108 (1914).

<sup>5</sup> "Parts per million" is abbreviated throughout to p.p.m.



culture of dist. water without salicylic aldehyde was included in the test and used as a control. The cultures grew from May 4th to May 16th, 1912. It became at once apparent that the salicylic aldehyde was very harmful to the seedling wheat, even in the lowest conc. of 10 p.p.m. The appearance of the series of plants on the 6th day is shown in Fig. 1 (Plate 6). In the culture solution containing 10 p.p.m., growth was reduced 31 percent; in the 25 p.p.m. solution growth was reduced 69 percent; with 50, 100 and 200 p.p.m. the plants were killed.

**EFFECT ON CORN.** The effect of salicylic aldehyde on corn plants was tested by growing the corn in nutrient solutions of calcium acid phosphate, sodium nitrate and potassium sulphate, with and without salicylic aldehyde. The aldehyde was used in amounts of 10, 25, 100, and 200 p.p.m. One corn plant was used in each culture jar containing 250 c.c. of the solution. The plants were germinated and put in the solution when they were about 1½ in. high. The corn grew in the solutions from May 26th to June 20th, 1912. A photograph of the cultures is shown in Fig. 2 (Plate 6), taken when the plants had been growing for 10 days. The harmfulness of this substance to corn is clearly shown. The effect was very noticeable, even in the culture containing 10 p.p.m. In the culture containing 200 p.p.m. there was very little growth; the plants were almost dead.

In Table 1 are given the green weights of the plants, taken when the experiment was concluded. The last column gives the relative growth.

TABLE 1

*Effect of salicylic aldehyde on corn in nutrient solutions of calcium acid phosphate, sodium nitrate and potassium sulphate*

No.	Treatment	Green weight	Relative growth
		gram	
1 Nutrient solution		1.00	100
2 " "	+ 10 p.p.m. salicylic aldehyde	0.60	60
3 " "	+ 25 p.p.m. " "	0.60	60
4 " "	+ 50 p.p.m. " "	0.21	21
5 " "	+ 100 p.p.m. " "	0.21	21
6 " "	+ 200 p.p.m. " "	0.10	10

The figures in Table 1 show the decreased growth due to the salicylic aldehyde. Ten p.p.m. reduced growth from 100 to 60 or 40 percent; 50 and 100 p.p.m. were also extremely harmful; there was very little growth in the presence of 200 p.p.m.

EFFECT ON COWPEAS. An experiment with cowpeas was made similar to that with corn seedlings, using the same conc. of salicylic aldehyde and the same nutrient solution. The plants grew in the solutions from June 15th to June 28th. One plant was used in each culture.

The effect of the aldehyde on the cowpea plants was similar to that with wheat and corn. In Fig. 3 (Plate 6) are shown the plants as affected by the aldehyde. From this it is seen that amounts larger than 10 p.p.m. were extremely harmful to the cowpeas.

In Table 2 are given the green weights of the cowpea plants taken at the end of the experiment.

TABLE 2

*Effect of salicylic aldehyde on cowpeas in nutrient solutions*

No.	Treatment	Green weight	Relative growth
		gram	
1 Nutrient solution		1.35	100
2 " "	+ 10 p.p.m. salicylic aldehyde	1.35	100
3 " "	+ 25 p.p.m. " "	0.70	51
4 " "	+ 50 p.p.m. " "	0.35	26
5 " "	+ 100 p.p.m. " "	0.20	15
6 " "	+ 200 p.p.m. " "	0.15	11

The figures in Table 2 show that salicylic aldehyde in amounts of 10 p.p.m. did not affect the green weight, which was the same in that culture as in the nutrient solution that did not contain aldehyde. The culture containing 25 p.p.m. of the aldehyde, however, produced a much smaller plant than the control. The growth was reduced from 100 to 51. Solutions containing 50, 100, and 200 p.p.m. produced very poor plants, which made very little growth and were almost dead when the experiment was discontinued.

EFFECT ON CABBAGE. An experiment in nutrient solution was made to study the effect of the salicylic aldehyde on young cabbage plants. The nutrient solution was the same as that used with corn and cowpeas. The salicylic aldehyde was used in varying quantities from 10 to 200 p.p.m. Ten young cabbage seedlings were grown in each culture. The plants grew in the solution from May 25th to June 12th, 1912. A photograph of the cultures was taken when they had grown 7 days; they are shown in Fig. 4 (Plate 6).

Ten and 25 p.p.m. materially reduced the growth, while 50 p.p.m. killed the plants. Cultures stronger than 50 p.p.m. are not shown.

When weighed at the termination of the experiment, growth in the culture containing 10 p.p.m. salicylic aldehyde was found to be reduced 30 percent. With 25 p.p.m. growth was reduced 61 percent. This shows that the aldehyde was quite harmful in small amounts to young cabbage plants; and in nutrient cultures containing 50, 100 and 200 p.p.m. of the aldehyde, the plants were killed.

EFFECT ON RICE. When tested on rice seedlings in water and in nutrient solutions, salicylic aldehyde was also found to be harmful to this crop. The dist. water solutions of 10 p.p.m. of salicylic aldehyde gave a depression of 16 percent in the green weight of the plants. In the nutrient solutions, the 10 p.p.m. of salicylic aldehyde gave a depression of 15 percent in the green weight.

## SOIL CULTURES

EFFECT ON WHEAT. Experiments were made to study the effect of salicylic aldehyde in soil. Paraffined wire pots, holding approximately one pound of soil, were used. The soil was a heavy clay loam. Before potting, portions of the soil were treated with different amounts of salicylic aldehyde. Six wheat plants were grown in each pot. The experiment was begun May 27th and discontinued June 18. In Fig. 5 (Plate 7) are shown the plants as they appear near the end of the experiment. This shows that the salicylic aldehyde was harmful. The final results are given in Table 3.

TABLE 3  
*Effect of salicylic aldehyde on wheat plants in soil*

No.	Treatment	Green weight	Relative growth
		gram	
1 Clay loam untreated		0.65	100
2 " " "	+ 10 p.p.m. salicylic aldehyde	0.65	100
3 " " "	+ 25 p.p.m. " "	0.50	77
4 " " "	+ 50 p.p.m. " "	0.40	61
5 " " "	+ 100 p.p.m. " "	Dead	—
6 " " "	+ 200 p.p.m. " "	Dead	—

As seen from the data in Table 3, the aldehyde in amounts of 10 p.p.m. had no effect in the soil. Larger amounts than 10 p.p.m.

were quite harmful. With 25 p.p.m. growth was reduced from 100 to 77, or 23 percent. With 50 p.p.m. growth was reduced from 100 to 61, or 39 percent. In amounts of 100 and 200 p.p.m. the plants were killed.

**EFFECT ON CORN.** The action of salicylic aldehyde in soil and also in sand was tested as to its effect on corn. The aldehyde was added to a clay soil and to pure quartz sand in amounts of 50 p.p.m. One pot each of the soil and sand untreated was run as a check. Corn was planted May 23d and it grew until June 20th. One corn plant was used in each pot containing soil and two plants in the pots containing sand.

A photograph of the plants is shown in Fig. 6 (Plate 7). The first two pots contain soil and the last two sand. Number 2 in each case is treated with salicylic aldehyde. Growth in the treated pots is seen to be much smaller than that in the check pots. The effect of the salicylic aldehyde in the sand is seen to be greater than in the clay soil.

The green weights of the plants were taken at the termination of the experiment. The salicylic aldehyde was found to have reduced growth in the clay soil from 100 to 76, or 24 percent, and in sand from 100 to 40, or 60 percent. The harmful effect was more marked in the quartz sand than in the clay soil, which is probably due to the absorptive power of the clay, being far greater than that of the sand, and perhaps also to the higher nutritive value of the soil in comparison with the pure sand.

**EFFECT ON CLOVER** The clover was grown in an ordinary flower pot holding 6 lbs. of soil; a good loam soil—the Hagerstown loam. One pot was untreated, the other had a total of 100 p.p.m. of the salicylic aldehyde added to it.

When the soil was potted, 50 p.p.m. of the aldehyde were added, and clover then sown, 0.5 gram of seed per pot. Later, when the clover was up, 25 p.p.m. more of the aldehyde were added in solution through a funnel passing into the soil nearly to the bottom of the pot, thus avoiding direct contact with the tops or roots of the clover. Three weeks later another 25 p.p.m. were added in the same manner. The experiment lasted from April 12th to June 21st, 1912. From the beginning the effect of the aldehyde on the clover was noticeable.

Fig. 7 (Plate 7) shows the appearance of the pots when the clover was well up and clearly indicates the inhibitory effect of the salicylic aldehyde. The control was of a deep green color, while the treated pot showed not only a poor growth, but also a much faded color and had a decidedly unhealthy appearance.

The green weights taken at the termination of the experiment were 8.5 gm. from the control pot and only 4.2 gm. from the salicylic-aldehyde-treated pot, a decrease of approximately 50 percent.

In the foregoing, salicylic aldehyde has been shown to be harmful to wheat and rice seedlings in distilled water, to wheat, corn, cowpeas, cabbage and rice in nutrient solutions, to wheat, corn and clover in soil in pots.

#### SOLUTION CULTURES WITH VARIOUS FERTILIZER INGREDIENTS

**EFFECT ON GROWTH.** The effect of salicylic aldehyde on wheat plants was further studied by growing the seedlings in nutrient culture solutions containing the ordinary fertilizer salts, calcium acid phosphate, sodium nitrate, and potassium sulphate, in various proportions. Some of the cultures contained calcium acid phosphate only, some sodium nitrate only and some potassium sulphate only. Other solutions were composed of mixtures of two salts, calcium acid phosphate and sodium nitrate, calcium acid phosphate and potassium sulphate, and sodium nitrate and potassium sulphate. Still other solutions had all three constituents in various proportions. The compositions of the various solutions are given in the first three columns of the tables which are to follow later.<sup>6</sup>

Two sets of cultures were prepared: to one set were added merely the nutrient salts; to a similar set 10 p.p.m. of salicylic aldehyde were added to each culture, in addition to the nutrient salts. The culture solutions were changed every three days, four changes being made in the course of the experiment. The solutions were analyzed for nitrates immediately after each change. The phosphate and potassium were determined on a composite solution of the four changes. The culture grew from May 15th to May 27th, 1912.

<sup>6</sup> The solutions were prepared as described in *Bul. 70, Bureau of Soils, U. S. Dep't Agri. (1910)*.



When the plants had grown for several days it was noticeable that the salicylic aldehyde cultures were developing slower. Each of the cultures seemed affected regardless of the composition or the proportion of the nutrient salts. When the plants had grown for 12 days with four changes of the solutions, the green weights were taken. The results obtained with the solution of different fertilizer ingredients are grouped in the tables to follow, so as to bring together those cultures which were composed principally of phosphate, those which were composed principally of nitrate, and those which were composed principally of potassium salts. In each group there were 21 cultures. A fourth group composed of six cultures is also given, which comprises the cultures with nearly equal proportions of the three salts.

Table 4 gives the growth in cultures composed principally of phosphate, without and with 10 p.p.m. of salicylic aldehyde. The composition of the culture solution is given in the first three columns. As will be seen, the solutions contain principally phosphate, but

TABLE 4

*Effect of salicylic aldehyde on wheat in nutrient culture solutions, composed principally of phosphate*

Composition of culture solution			Without salicylic aldehyde	With salicylic aldehyde: 10 p.p.m.
P <sub>2</sub> O <sub>5</sub>	NH <sub>3</sub>	K <sub>2</sub> O	Green weight	Green weight
p.p.m.	p.p.m.	p.p.m.	grams	grams
80	0	0	1.02	0.76
72	0	8	1.32	1.04
72	8	0	1.30	1.14
64	0	16	1.32	1.22
64	8	8	1.70	1.44
64	16	0	1.54	1.14
56	0	24	1.24	1.28
56	8	16	2.34	1.52
56	16	8	2.04	1.66
56	24	0	1.34	1.28
48	0	32	1.62	1.22
48	8	24	2.50	1.54
48	16	16	2.60	1.92
48	24	8	2.50	1.88
48	32	0	1.64	1.34
40	0	40	1.75	1.10
40	8	32	1.90	1.52
40	16	24	2.98	2.16
40	24	16	2.88	2.14
40	32	8	2.28	1.74
40	40	0	1.80	1.60

also different smaller amounts of nitrate and potash stated in p.p.m. of  $P_2O_5$ ,  $NH_3$  and  $K_2O$ . In the fourth column is given the green weight of the plants grown in solutions which contain no salicylic aldehyde, and in the fifth column is given the weight of the plants in solutions which contain 10 p.p.m. of salicylic aldehyde.

By comparing the two last columns in Table 4 it is seen that the green weight of the salicylic aldehyde culture is less in every case, with one exception only, than the green weight of the culture of the same fertilizer mixture without the salicylic aldehyde. The total green weight of the 21 normal or control cultures was 39.61 gm. against 31.74 gm. for the 21 cultures with salicylic aldehyde.

Table 5 gives the data for effects of salicylic aldehyde in nutrient solution in which the principal ingredient is nitrate.

TABLE 5

*Effect of salicylic aldehyde on wheat in nutrient culture solutions, composed principally of nitrate*

Composition of culture solution			Without salicylic aldehyde	With salicylic aldehyde: 10 p.p.m.
$P_2O_5$	$NH_3$	$K_2O$	Green weight	Green weight
p.p.m.	p.p.m.	p.p.m.	grams	grams
0	80	0	1.80	1.31
0	72	8	2.00	1.60
8	72	0	1.86	1.30
0	64	16	2.00	1.50
8	64	8	2.50	1.84
16	64	0	1.76	1.40
0	56	24	2.04	1.74
8	56	16	3.00	1.73
16	56	8	2.24	2.04
24	56	0	1.72	1.54
0	48	32	2.60	1.82
8	48	24	3.12	1.60
16	48	16	2.74	1.74
24	48	8	2.34	2.00
32	48	0	1.80	1.55
0	40	40	2.50	1.54
8	40	32	3.44	2.12
16	40	24	3.00	2.10
24	40	16	2.70	2.10
32	40	8	2.20	1.88
40	40	0	1.80	1.60

As seen in the fourth and fifth columns of Table 5, the growths in cultures with salicylic aldehyde are much smaller than the growths in solutions containing merely the nutrient salts. The total green

weight of the 21 cultures in nutrient salts was 49.36 gm. and the green weight of the 21 nutrient cultures containing 10 p.p.m. salicylic aldehyde was only 36.11 gm. From these figures it is seen that salicylic aldehyde in these nutrient solutions (principally nitrogenous), as in the phosphate solutions, is quite harmful to wheat plants.

Table 6 gives the effect of salicylic aldehyde in cultures that are principally potassic, as does Table 4 for the phosphate cultures and Table 5 for the nitrate cultures.

TABLE 6

*Effect of salicylic aldehyde on wheat in nutrient culture solutions, composed principally of potash*

Composition of culture solution			Without salicylic aldehyde	With salicylic aldehyde: 10 p.p.m.
P <sub>2</sub> O <sub>5</sub>	NH <sub>3</sub>	K <sub>2</sub> O	Green weight	Green weight
p.p.m.	p.p.m.	p.p.m.	grams	grams
0	0	80	1.30	0.90
0	8	72	1.32	1.48
8	0	72	1.30	1.14
0	16	64	2.20	1.42
8	8	64	2.20	1.62
16	0	64	1.46	1.18
0	24	56	2.22	1.50
8	16	56	3.00	2.24
16	8	56	2.52	1.74
24	0	56	1.60	1.10
0	32	48	2.32	1.70
8	24	48	3.25	2.02
16	16	48	2.42	1.90
24	8	48	2.40	1.44
32	0	48	1.54	1.15
0	40	40	2.50	1.54
8	32	40	3.15	2.34
16	24	40	2.32	2.08
24	16	40	3.20	2.05
32	8	40	2.70	1.70
40	0	40	1.75	1.10

From Table 6 it is seen that the aldehyde cultures are much smaller than the normal cultures. The total green weight of the 21 normal cultures was 47.67 gm. against 33.74 gm. for the cultures containing the salicylic aldehyde.

The six cultures composed of approximately equal amounts of P<sub>2</sub>O<sub>5</sub>, NH<sub>3</sub>, and K<sub>2</sub>O are given in Table 7. The total green weight of the cultures in nutrient salts without salicylic aldehyde was 18.92

gm., and the total green weight for the cultures of similar composition with 10 p.p.m. salicylic aldehyde was 12.37 gm.

TABLE 7

*Effect of salicylic aldehyde on wheat in nutrient culture solutions, composed of phosphate, nitrate and potash*

Composition of culture solution			Without salicylic aldehyde	With salicylic aldehyde: 10 p.p.m.
P <sub>2</sub> O <sub>5</sub>	NH <sub>3</sub>	K <sub>2</sub> O	Green weight	Green weight
p.p.m.	p.p.m.	p.p.m.	grams	grams
32	16	32	2.94	1.86
32	24	24	3.12	2.30
32	32	16	2.84	1.97
24	24	32	3.68	2.04
24	32	24	3.00	2.00
16	32	32	3.34	2.20

From the foregoing results it is seen that salicylic aldehyde, in amounts as small as 10 p.p.m., is harmful to the growth of wheat in culture solutions. In regard to the composition of the nutrient solutions affecting the harmfulness of the aldehyde, it might be said that an analysis of the total green weights obtained in the case of the mainly phosphatic, the mainly nitrogenous and the mainly potassic fertilizers, given in Tables 4, 5 and 6, respectively, shows that the least harmful effects occurred in the phosphatic group of cultures. This group as a whole shows a depression due to salicylic aldehyde of approximately 20 percent in growth, while the other two groups showed approximately 27 and 29 percent below the respective group of cultures without the aldehyde.

**EFFECT ON ABSORPTION OF NUTRIENT SALTS.** As salicylic aldehyde has been shown to be harmful to growth in culture solutions containing nutrient salts, it will be interesting to study its effect on the removal of nutrients from the solution during the growth of the plant.

As stated above the concentration differences produced by the growth of the plants in the various cultures were determined by making an analysis for nitrates at the termination of every three-day change, and of phosphate and potassium on a composite of the solutions from the four changes.<sup>7</sup> It becomes possible, therefore,

<sup>7</sup> These determinations were made colorimetrically as described in *Bul. 31* and *Bul. 70, Bureau of Soils, U. S. Dep't Agri.*

to compare the results obtained in the normal cultures without salicylic aldehyde and in the cultures where 10 p.p.m. of salicylic aldehyde were present in the solution.

The sum total of  $P_2O_5$ ,  $NH_3$  and  $K_2O$  removed from solution by the growing plants in all of the cultures under study was 1646.6 mg. in the normal cultures and 1332.3 mg. in the nutrient cultures containing salicylic aldehyde. The figures show the total of plant nutrients removed to be less in the cultures containing salicylic aldehyde than in the normal cultures, which indicates that the salicylic aldehyde cultures used less nutrients than the normal. An examination of the results pertaining to the three constituents separately are given below.

*Phosphate.* The amount of phosphate, stated as  $P_2O_5$ , that was removed from the total number of solutions during the experiment was 395.7 mg. for the normal cultures and 344.2 mg. for the cultures containing salicylic aldehyde. The salicylic aldehyde cultures absorbed 51.5 mg. of  $P_2O_5$  less than the normal cultures.

*Nitrate.* The total amount of nitrate, stated as  $NH_3$ , that was removed from the total number of solutions during the course of the experiment was 578.3 mg. for the normal cultures and 454.9 mg. for the salicylic aldehyde cultures. The salicylic aldehyde cultures used 123.4 mg. less nitrate.

*Potassium.* The amount of potash, stated as  $K_2O$ , that was absorbed by the plants in the total number of cultures was 672.6 mg. in the case of the normal cultures and 533.2 mg. for the cultures with salicylic aldehyde. As with the phosphate and nitrate, the salicylic aldehyde cultures absorbed less potash, there being a difference of 139.4 mg. in favor of the normal cultures.

An examination of the above figures shows a more nearly normal absorption of phosphate than of the nitrate or potash under the influence of the salicylic aldehyde. This would appear to be in harmony with the relatively lessened toxicity of the aldehyde in the mainly phosphatic nutrient solutions.

EFFECT OF CALCIUM CARBONATE ON THE ACTION OF SALICYLIC ALDEHYDE. In order to study the physiological effect of salicylic aldehyde under alkaline conditions, an experiment was made in nutrient culture solutions containing calcium carbonate. The cul-



tures were prepared as in the experiments already recorded. The solutions were composed of calcium acid phosphate, sodium nitrate and potassium sulphate in different proportions. Salicylic aldehyde was used in quantities of 10 p.p.m., and 100 mg. of calcium carbonate were added to each culture, in the control set and in the salicylic aldehyde set. The plants grew from Mar. 23d to April 4th—12 days. The solutions were changed every 3 days. The green weights of the plants grown in solution without and with salicylic aldehyde are given in the two last columns of Table 8.

TABLE 8

*Effect of salicylic aldehyde in nutrient cultures containing calcium carbonate*

Composition of nutrient solution			Without salicylic aldehyde	With salicylic aldehyde: 10 p.p.m.
P <sub>2</sub> O <sub>5</sub>	NH <sub>3</sub>	K <sub>2</sub> O	Green weight	Green weight
p.p.m.	p.p.m.	p.p.m.	grams	grams
48	16	16	2.85	1.95
64	8	8	2.00	1.95
16	48	16	3.19	2.45
8	64	8	2.70	2.45
16	16	48	3.55	2.55
8	8	64	3.60	2.05

These data show that salicylic aldehyde was harmful even in nutrient solutions containing an excess of lime. The growth in each culture with salicylic aldehyde was less than the corresponding culture containing no salicylic aldehyde. The total growth of the six control cultures was 17.89 gm. against 13.4 gm. for the six salicylic aldehyde cultures. Putting the normal at 100, the salicylic aldehyde cultures become 75, a reduction in growth of 25 percent.

In another test involving a much larger number of cultures of different composition, essentially the same result was obtained. In this case the growth was depressed 21 percent as an average.

In the previous experiment involving a larger number of nutrient solutions without calcium carbonate, growth was reduced 27 percent by salicylic aldehyde, used in the same conc. as for the experiment with calcium carbonate.

The roots of the plants were not as much stunted by the salicylic aldehyde in the presence of calcium carbonate as they were in the

experiment when no calcium carbonate was used. The tops, however, were still much affected in the carbonate cultures.

From these experiments under alkaline conditions it is seen that the harmfulness of salicylic aldehyde can not be attributed to any slight acidity it may possess. There is some indication that calcium carbonate ameliorated its effects.

## EXPLANATION OF PLATES

SKINNER: EFFECT OF SALICYLIC ALDEHYDE ON PLANTS IN SOIL, AND  
SOLUTION CULTURES

### Plate 6

*Fig. 1: Effect of salicylic aldehyde on wheat seedlings in water sol.* (1) Control in dist. water; (2) same, plus salicylic aldehyde, 10 p.p.m.; (3) 25 p.p.m.; (4) 50 p.p.m.; (5) 100 p.p.m.; (6) 200 p.p.m.

*Fig. 2: Effect of salicylic aldehyde on corn plants in nutrient sol.* (1) Control in nutrient sol.; (2) same, plus salicylic aldehyde, 10 p.p.m.; (3) 25 p.p.m.; (4) 50 p.p.m.; (5) 100 p.p.m.; (6) 200 p.p.m.

*Fig. 3: Effect of salicylic aldehyde on cowpea plants in nutrient sol.* (1) Control in nutrient sol.; (2) same, plus salicylic aldehyde, 10 p.p.m.; (3) 25 p.p.m.; (4) 50 p.p.m.; (5) 100 p.p.m.; (6) 200 p.p.m.

*Fig. 4: Effect of salicylic aldehyde on cabbage plants in nutrient sol.* (1) Control in nutrient sol.; (2) same, plus salicylic aldehyde 10 p.p.m.; (3) 25 p.p.m.; (4) 50 p.p.m.

### Plate 7

*Fig. 5: Effect of salicylic aldehyde on wheat in soil.* (1) Clay loam untreated; (2) same, plus salicylic aldehyde, 10 p.p.m.; (3) 25 p.p.m.; (4) 50 p.p.m.; (5) 100 p.p.m.

*Fig. 6: Effect of salicylic aldehyde on corn in soil and in sand.* (A)—Clay loam soil: (1) Untreated; (2) salicylic aldehyde, 50 p.p.m.; (B)—Sand: (1) Untreated; (2) salicylic aldehyde, 50 p.p.m.

*Fig. 7: Effect of salicylic aldehyde on clover in soil.* (1) Soil untreated; (2) soil with a total of 100 p.p.m. of salicylic aldehyde.



SKINNER: EFFECT OF SALICYLIC ALDEHYDE ON PLANTS IN SOIL, AND SOLUTION CULTURES





SKINNER: EFFECT OF SALICYLIC ALDEHYDE ON PLANTS IN SOIL, AND SOLUTION CULTURES





# ON THE PHOSPHORUS CONTENT OF STARCH\*

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The fact that starch contains phosphorus has been known for a long time but, strange to say, very little work has been done to determine the relation of the phosphorus to the starch.

Fouard,<sup>1</sup> while studying the colloidal properties of starch, made some interesting determinations of its phosphorus content. He made soluble starch from raw starch by the Lintner process: this he called No. 1; and, by acid treatment of this portion, he made a second preparation of soluble starch: No. 2; and so on until, by successive acid treatments, he had five specimens of soluble starch. All were washed free from acid. He incinerated portions of each and determined the phosphoric anhydrid in the ash. Starting with a starch whose phosphorus content was 0.0724 percent, his fifth purified sample contained 0.0422 per cent. He reported the following results:

	Initial starch	Soluble starch 1	2	3	4	5
Percent of ash.....	0.3310	0.1950	0.1715	0.1450	0.1260	0.1240
Percent of $H_3PO_4$ .....	0.1915	0.1318	0.1177	0.1148	0.1210	0.1117

It is interesting to note that in the purest sample the ash consisted almost wholly of phosphoric acid, but that, as the starch became purer, the percentage of ash decreased from 0.331 percent to 0.124 percent while the phosphoric acid decreased only from 0.1915 percent to 0.1117 percent. This seems to indicate that the phosphorus was present in chemical combination with the starch. Fouard, however, does not believe this to be the case. He made titrations of the total acidity toward methyl orange and phenol-

\* Proceedings of the Columbia Univ. Biochem. Assoc. (16th meeting, Feb. 6, 1914).

<sup>1</sup> Fouard: *Compt. rend.*, 1907, cxliv, p. 501.

phthalein indicators: and, due to a rough difference in the titrations with the two indicators (the difference was not constant), he claimed that the phosphorus was present in the form of phosphoric acid. He said that if it were in organic combination no acid reaction would be manifested.

Ford,<sup>2</sup> in the course of diastase studies, attempted to free starch from "phosphates," by reprecipitating several times from acid solution by means of alcohol. He found, however, that he could not entirely remove the phosphorus compound, his purest preparation of starch containing 0.1 percent phosphoric anhydrid. The aqueous solution of this starch was neutral to rosolic acid and methyl orange.

Now, if Fouard's view that phosphorus is present in starch as free phosphoric acid is true, why can it not be washed out? Why, in his own purification experiments, did the gross weight of ash decrease 62 percent while the phosphoric acid (determined in the ash) decreased only 41 percent? Surely, if starch is not combined chemically with the phosphorus, its hold in the preparations is astonishingly tenacious.

Purification experiments conducted in this laboratory confirm Ford's and Fouard's experiences in that it is impossible to free starch entirely from phosphorus.

On Oct. 27 twelve medium sized potatoes were macerated, the starch separated and kept under water and toluene until Nov. 3, when starch from twenty-four freshly macerated potatoes was added to the first portion. The starch was washed by decantation and shaking with 4-5 liters of hydrant water several times each day until Nov. 10. On Nov. 10 the product was dried between filter papers in the draught of an electric fan until Nov. 11 (Sample A), when 490 gm. were placed in 5 liters of 7 percent hydrochloric acid sol. and shaken vigorously in order to convert the raw starch to soluble starch. This shaking was repeated twice daily until Nov. 18, when the acid sol. was poured off and dist. water was substituted for it. Fresh dist. water was added daily, and by Nov. 25 the washings were neutral to litmus (Sample B). From Nov. 25 to Dec. 15 (taking Sample C on Dec. 1 and Sample D on Dec. 8) the starch was washed by decantation and shaking with 2 liters of dist. water twice daily.

<sup>2</sup> Ford: *Jour. Soc. Chem. Ind.*, 1904, xxiii, p. 414.

On Dec. 15 the starch was placed in an oven to dry. Unfortunately it was too wet and some of it jellied. It then had to be slowly dried until Dec. 22, when it was ground up to 100 mesh and put into distilled water for a day's further washing. On Dec. 23 drying before a fan was started and on Dec. 27, after the process had been completed, the product was placed in an oven at 105° C. for 4 hr., and then bottled (Sample E.)

This final soluble starch product was so pure that it could not be precipitated from water by alcohol. A 3 percent sol. was made by adding the required amount of paste to boiling water and then cooling. To some of this sol. an equal vol. of alcohol was added with the result that a milky suspension but no separable precipitate was formed. Ordinary soluble starch is precipitable by alcohol due to the presence of electrolytes as impurity. Traces of electrolyte cause precipitation. In order to see what the behavior of the phosphorus compound would be, a drop or two of 10 percent sodium chlorid sol. was added to 200 cc. of 3 percent sol. and then the starch was precipitated by means of 200 cc. of alcohol. About 2.5 gm. were obtained. This precipitate (Sample F) was dried and analyzed for phosphorus. The phosphorus figures are summarized below:

Sample.....	A	B	C	D	E	F
Percent $P_2O_5$ .....	0.1227	0.1118	0.1084	0.0378	0.0378	0.035
Percent P.....	0.0536	0.051	0.0473	0.0168	0.0168	0.0153

It is interesting to note that *E* contains 0.0168 percent of phosphorus. This starch gives a true *colloidal dispersion in water which is not precipitable by alcohol; evidence that very little if any electrolyte is present*. Therefore, all the phosphorus cannot be present as  $H_3PO_4$  as Fouard claims, and our only other assumption can be that the phosphorus is present in some *un-ionized* form, *i. e.*, in organic combination with the starch.

It is also of interest to note that Sample F, the electrolyte-alcohol precipitate of a solution of E, contains (within the limits of experimental error) practically the same amount of phosphorus as Sample E. This would seem to bear out our point that the phosphorus is not *all* occluded as phosphoric acid. If it were only mechanically

held by the starch granules why should *all* of it be precipitated with the starch while other ash constituents are not so reprecipitated?

If our assumption that the starch of Sample F is all in chemical combination with phosphorus is correct, then we might estimate the molecular weight of starch from the proportion  $0.0153:31 = 100:x$ , to be about 200,000.

These observations extend the work, under Dr. Gies' guidance, which was lately reported by Mattill.<sup>3</sup>

<sup>3</sup> Mattill: *BIOCHEM. BULL.*, 1913, ii, p. 553.



# A STANDARD FOR THE DETERMINATION OF AMMONIA BY MEANS OF NESSLER SOLUTION

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The determination of nitrogen is one of the most frequent and valuable operations for the investigation of substances and processes of animals and plants. The method of Kjeldahl has been a tool of inestimable value to the biological chemist and it has had comparatively few limitations in his hands. There are times, however, when the available amount of material for analysis is so small that the chemist resorts to the method grudgingly or must perforce omit it entirely. This limitation has now been removed by the modifications of Folin and his pupils, whereby the operation can be conducted on relatively minute quantities.

For the measurement of the ammonia produced by the Kjeldahl-Gunning digestion, Folin<sup>1</sup> uses the Nessler-Winkler solution, so familiar in sanitary laboratories. To match the colors produced by the ammonia from the substance examined, and from the standard ammonium sulfate, the Duboscq colorimeter is employed. The method appealed to the workers in this laboratory, where the determination of the nitrogen distribution in small samples has been an impending trouble. We trust that part of our experience with it, which we now publish, may be of assistance to other beginners in the application of this promising method.

There are several procedures in making up the Nessler reagent. The results of all these may be the same, but the one selected has been adhered to throughout in order to obviate all chances of further variation. The reagent is prepared as follows: 62.5 gm. of potassium iodid are dissolved in 250 c.c. of water, to which is added a saturated sol. of mercuric chlorid, with stirring until a permanent

<sup>1</sup> Folin and Farmer: *Jour. Biol. Chem.*, 1911, ix, p. 493; Folin: *Ibid.*, pp. 507-525.

precipitate is formed, care being taken not to pass this point. Then, 150 gm. of potassium hydroxid, dissolved in 250 c.c. of water, are added to the iodide sol. and the mixture is then diluted to 1 liter. In nesslerizing, a portion of this sol. is diluted five times and 35 c.c. are used.

There are conditions which influence greatly the ease with which nesslerized solutions may be matched. Even in following closely the same procedure there are frequently striking variations. There may be times when the readings, in large numbers, do not vary more than 0.1 mm.; at other times, under apparently identical conditions, it has been necessary to average readings with a maximum variation of as much as 1 mm. This irregularity led the authors to study the limits of errors in nesslerizing with the Duboscq colorimeter and also to seek a more stable standard.

A number of yellow and red solutions were tried singly and in combination. At the suggestion of Mr. A. M. Buswell, of the Department of Sanitary Engineering, Columbia University, the papers of Jackson and Richards were referred to.<sup>2</sup> These authors give us a standard now used extensively in sanitary laboratories, consisting of mixtures of solutions of potassium platonic chlorid and cobalt chlorid in hydrochloric acid. These colors did not match our standard made from an ammonium sulfate sol. containing 1 mg. per c.c., but the reading of the papers suggested chloroplatinic acid, which was tried. A 21 percent sol. of this acid just matches our standard ammonium sulfate sol. to which the Nessler reagent has been added and allowed to stand for 20 min. It was found, however, that this expensive solution could be replaced by a five percent sol. of chloroplatinic acid to which was added one-half its vol. of hydrochloric acid sol. containing 1.2 percent of cobaltic chlorid.

The readings are as easily discerned in using this standard as in the case of ammonium sulfate sol. to which Nessler reagent has been added. In this case, as in the other referred to above, there are conditions not yet determined under which it is difficult to get readings within the limits of 0.2 mm. This difficulty may be due to the formation of molecular aggregates that induce irregular transmission of the light, as is suggested by the illusive opalescence which

<sup>2</sup> Jackson: *Tech Quart.* 1900, xiii, p. 320; Richards and Miller; *Ibid.*, 1904, xvii, p. 277.

sometimes develops in solutions of low  $\text{NH}_4$  content and by the ferric hydrate-like precipitate formed when the ammonium salt is present in two large amounts for nesslerizing. The chemist should also be cautioned against a high reading due to the same source of error, in which there is a partial exclusion of the light by colloidal particles on the borderline between suspension and true solution.

In our experience, this adaptation or modification of the method is very accurate for solutions whose nitrogen content ranges from 0.0004 to 0.002 gm. per c.c.

TABLE I

*Data pertaining to the accuracy of the readings*

Amount of nitrogen in sol., per c.c.	Time of color development	Maximum variation of the readings	Average reading	Theoretical reading based on a large no. of determinations
mg.	min.	mm.	mm.	mm.
0.505	10	0.3	46.1	46.0
	15	0.0	45.9	46.0
	20	0.2	45.9	46.0
0.808	10	0.0	29.9	28.7
	10	0.1	28.8	28.7
	15	0.1	28.8	28.7
	20	0.3	28.7	28.7
1.01	10	0.4	23.0	23.0
	10	0.0	23.0	23.0
	15	0.3	23.0	23.0
	15	0.3	22.8	23.0
	20	0.4	23.0	23.0
1.212	10	0.1	19.0	19.1
	15	0.0	19.1	19.1
	20	0.1	19.0	19.1
1.515	10	0.4	15.1	15.1
	15	0.2	15.1	15.1
	20	0.4	15.1	15.1
2.02	10	0.2	12.7	11.5
	15	0.1	11.2	11.5
	20	0.0	11.5	11.5
	20	0.2	11.4	11.5

Our practice has been to place the cup containing the cobalt-platinum sol. at the 20 mm. point and to move the other cup so as to get three readings moving down, and three in the upward direction. The solution should be standardized to each arbitrary mark selected for the readings. Though the readings are accurate

through a fairly wide range of mm., it is advantageous to have a diluter solution on hand for samples very low in nitrogen content. If this solution is obtained by diluting the stronger standard, its nitrogen equivalent is not in proportion to the dilution and must be obtained by comparing the same with a nesslerized standard ammonium sol. Fifteen minutes are allowed to develop the color and the readings are taken within ten minutes after this time. Table 1 gives the results of one set of readings on standard ammonium sulfate, which was used to determine the time element and the amount of Nessler reagent most advantageous for the best results. Additional data are given in Table 2.

TABLE 2

*A comparison of data obtained by the micro method and the Kjeldahl Gunning method*

Sample No.	Micro method: platinum-cobalt standard Grams	Micro method: titration with $\pi/50$ acid Grams	Kjeldahl method: titration with $\pi/10$ acid Grams
P I	0.404	0.405	0.402
P II	0.794	0.794	0.793
C 27	1.246	1.247	1.245
C 28	1.005	1.021	1.012
C 29	1.120	1.124	1.117
C 30	1.148	1.149	1.148
H 186	0.410	0.413	0.414
H 189	0.688	0.688	0.688
Cas. FA, 45	0.113	0.113	0.115
Cas. FA, 30	0.682	—	0.685
U 59	0.996	—	0.997

## A MICRO-UREASE METHOD FOR THE DETERMINATION OF UREA

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The discovery by Takeuchi,<sup>1</sup> that from the soja bean (*Glycine hispida*) an enzyme can be extracted whose specific action is the conversion of urea into ammonium carbonate, offered the biological chemist a new means of determining this characteristic urinary constituent, which was not long delayed in application. The earliest attempts at the estimation of urea by this agent are those of Marshall.<sup>2</sup> More recently the properties of the enzyme have been studied by Van Slyke and Cullen,<sup>3</sup> who have given us a procedure by which it can be concentrated as a convenient soluble powder, and have also described a method of determining urea quantitatively by means of urease.

The possibility of adapting these methods to the work of this laboratory on the chemistry of bacteria, where only minute quantities or very small samples might be expected, led to a series of experiments that may be described here with profit.

The original plan gave very encouraging results and may be briefly stated as follows: The soja bean was finely ground, passed through a 20-mesh sieve, and placed in a stoppered bottle. When a determination or a series of determinations was to be made, 1 gm. of this flour was kept in 10 c.c. of water for an hour, with occasional shaking, and then either filtered or centrifuged. An amount of the solution in which the urea was to be determined was carefully pipetted into a Jena test tube. To this was added 2 c.c. of the

<sup>1</sup> Takeuchi: *Jour. Coll. Agric., Univ. Tokio*, 1909, i, p. 1. For earlier reference see Marshall's first paper cited below.

<sup>2</sup> Marshall: *Jour. Biol. Chem.*, 1913, xiv, p. 283; xv, p. 495.

<sup>3</sup> Van Slyke and Cullen: *Proc. Soc. Exp. Biol. Med.*, 1913, ix, p. 57. See also Armstrong and Horten: *Proc. Roy. Soc. Lond.*, 1913, lxxxvi, p. 328; Kiesel: *Zeit. physiol. Chem.*, 1911, lxxv, p. 169.



extract and a few drops of toluene, and the tube placed in an incubator at 37° C. The resultant ammonia was then determined by the aspiration method.

When this method was put into practice the authors were surprised to find that the hydrolysis of the urea was complete in less than 5 min. when the mixture was heated to 30–40° C. Tubes containing the mixture were kept for various lengths of time at room temperature; some also in a cold room at 0° C. The latter, after a period of 24 hr., gave results that were identical with those for the incubated mixtures, but yielded higher values than did those kept at room temperature (for 1–2 hr.), so there must have been considerable enzyme action under even these conditions. The incubator was, therefore, dispensed with and the tubes merely heated to 40–50° C. by immersing them in a pan of warm water at the time of aspiration. Preliminary extraction of the flour with ether was of no advantage nor was anything gained by using warm water. The period of soaking could not be shortened without reducing the strength of the extract.

The most troublesome feature of the work was the persistent frothing of the mixture during its aspiration. Toluene and petroleum oil were of no avail. Alcohol prevented the foaming for a time, but not permanently. The addition of a small piece of camphor reduced the surface tension sufficiently to permit aeration to proceed in a very satisfactory manner when tall cylinders and a vigorous air current were employed, but in the micro apparatus, this substance was sometimes carried over and interfered with the determination. The heavier paraffin oils were efficient, but at best rather disagreeable to use. The amyl and octyl alcohols proved very satisfactory, and in the micro apparatus, 0.5 c.c. of either of these is now used.

The surprising activity of the extract naturally suggested the simplification of the work by introducing the bean flour directly into the solution to be examined for its urea content. This part of the work was undertaken with some misgivings and first tried on urine samples in Folin's macro ammonia apparatus. The results were very gratifying and repeated in the micro apparatus with entire success.

As a result of this study, two procedures have been adopted in this laboratory.<sup>4</sup>

I. The micro-urease method is used in determining urea in small samples or when the amount of this substance is present in only minute quantities. Into a  $22 \times 200$  mm. test tube, the solution to be analyzed is carefully pipetted in an amount not exceeding 5 c.c., and containing not more than 2 mg. of nitrogen in the form of ammonia and urea. When only 1 c.c. is used, 2 c.c. of water are also added. If the solution is acid, it should be neutralized. Then 0.2–0.4 gm. of the bean flour is added and the mixture stirred, 0.5 c.c. of amyl or octyl alcohol run in, the tube attached to the apparatus, and aeration started. Under the tubes is placed a narrow pan into which is poured some water warmed to  $50-60^{\circ}$  C. In 5 min. the reaction is complete. To facilitate the removal of ammonia, 1–2 c.c. of saturated sodium carbonate sol. is drawn into the tube. The time of aspiration under the conditions prevailing in our laboratory need not exceed 35 min.

[The experience of this laboratory, as to the time required for the removal of the ammonia from a solution by aeration in micro and macro determinations of nitrogen and ammonia, does not agree with the published statements of Folin and his co-workers. In the latter six hours are usually required and in the former not less than thirty minutes. Sjoquist<sup>5</sup> presents data in harmony with this and also notes that the time may be materially shortened by warming the solutions. These variable time requirements are due to local conditions and should be tested in each laboratory where the methods are used.]

The receiving pipette is removed, the acid previously placed in it diluted to about 75 c.c., Nessler reagent added and then, after mixing, made up to the mark and matched against the appropriate platinum standard in the Duboscq colorimeter or titrated with  $n/50$  solutions. From these readings is subtracted the readings previously obtained for ammonia nitrogen, and the urea nitrogen calculated.

When the nitrogen of the sample taken is less than 0.4 mg., it is

<sup>4</sup> A paper by Plimmer and Skelton in a recent issue of the *Biochemical Journal* (viii, p. 70) is in close agreement with the subject matter treated in this paper.

<sup>5</sup> Sjoquist: *Sv. Kem. Tidskr.*, 1913, xxv, p. 167. Cf. *C. A.*, 1914, viii, p. 743.

advisable to add the equivalent of 0.5 or 1 mg. of nitrogen, in the form of a standard ammonium salt sol. at some time before nesslerizing, and then to subtract this amount from the final reading.

II. In metabolism work and general routine, where the samples are ample and the urea is present in fairly large amounts, the second procedure, which is a *macro method*, is employed. The Folin

TABLE I

*Comparative data pertaining to method for the determination of urea*

No.	Sample	Method	Titration cc. $\pi/10$	Nessleration mm.	N per cc. mg.
1 <sup>1</sup>	Urea sol.	Micro-urease	—	23.0	1.01
2	Urine, monkey (V, 1)	Folin micro	—	19.8 $\pm$ 0.0	2.35
				19.9 $\pm$ 0.1	2.34
3	do	Macro-urease	7.9	—	2.26
4	do	Micro-urease	—	19.8 $\pm$ 0.2	2.35
5 <sup>2</sup>	do	do	—	19.7 $\pm$ 0.1	2.37
6 <sup>3</sup>	Urine, dog (IV)	Macro-urease	48.0	—	13.73
7 <sup>3</sup>	do	do	50.5	—	14.44
8 <sup>3</sup>	do	do	51.0	—	14.74
9	do	Benedict	55.0	—	15.08
10	Urine, human (118)	Macro-urease	14.0	—	4.10
11	do	do	14.0	—	4.10
12	do	Benedict	13.6	—	3.89
13	do	do	13.7	—	3.92
14 <sup>2</sup>	Urine, human (123)	Micro-urease	—	17.85 $\pm$ 0.1	13.00
15 <sup>2</sup>	do	Folin micro	—	18.05 $\pm$ 0.1	12.06
16	Urine, human (127)	Macro-urease	31.5	—	9.01
17	do	Benedict	32.3	—	9.24
18	Urine, human (126)	Macro-urease	18.95	—	5.43
19	do	Benedict	19.25	—	5.51
20	Urine, human (128)	Macro-urease	28.6	—	8.18
21	do	Benedict	29.75	—	8.51
22 <sup>4</sup>	Urine, human (136)	Macro-urease	26.4	—	7.55
23 <sup>4</sup>	do	Benedict	26.3	—	7.52
24 <sup>4</sup>	Urine, human (131)	Macro-urease	10.4	—	2.97
25 <sup>4</sup>	do	Benedict	10.4	—	2.97
26 <sup>4</sup>	Urine, human (132)	Macro-urease	25.7	—	7.35
27 <sup>4</sup>	do	Benedict	25.6	—	7.32

<sup>1</sup> This solution (1) was made up to try the micro apparatus and has been analyzed a large number of times by several methods. It contains 1.01 mg. of ammonia nitrogen per c.c.

<sup>2</sup> These figures (5) represent thirteen determinations in which there were minor variations. On these over seventy readings were made, of which the maximum was 20.3 and the minimum 19.3. (Nos. 14 and 15 represent six determinations.)

<sup>3</sup> In 6, 7, and 8 the period of aeration was lengthened for each successive determination.

<sup>4</sup> In numbers 22 *et seq.*, the urine cylinders were kept warm the first half hour and the aspiration continued for a period two-fifths longer than that for the ammonia determinations by Folin's method.

ammonia apparatus is used and ammonia may be determined at the same time. After the cylinder has been slightly warmed, 5 c.c. of the sample and 30 c.c. of water warmed to 50–60° C. are introduced, and then about 5 gm. of the soja bean flour added. At the end of 30 min., about 5 c.c. of a saturated sol. of sodium carbonate are drawn into the cylinder containing the sample. The air current, which is passed through the apparatus continuously after the addition of the bean flour, is maintained until all the ammonia is transferred to the cylinder containing the standard acid sol., after which the excess of acid is titrated in the usual manner. Crude petroleum is used to prevent the frothing.

The accompanying table (1–2) give the data on which these two procedures are based.

TABLE 2

*Comparative data pertaining to methods for the determination of urea<sup>1</sup>*

Sample No.	Folin micro method Grams N	Micro-urease method Grams N	Macro-urease method Grams N	Benedict method Grams N
I	0.332	0.327	0.326	0.326
II	0.691	0.703	0.686	0.682
27	1.130	1.130	1.203	1.125
28	0.921	0.918	0.926	0.917
29	1.024	1.021	1.015	1.011
30	1.077	1.077	1.058	1.063
H 186	0.350	0.350	0.354	0.355
H 187	0.583	0.585	0.588	0.602
L 118	1.290	1.300	—	—
M I	—	—	0.754	0.752
M II	—	—	0.300	0.302
M III	—	—	0.743	0.741

In noting the difference in the readings on the colorimeter, the sign  $\pm$  is used in the accompanying table to indicate this variation. With Folin's micro method and the micro-urease method the results are always in close agreement. The method of Benedict always gives a trifle more nitrogen than the macro-urease method unless *every precaution* is taken to have all the ammonia transferred from the urine cylinder to the standard acid cylinder in the latter case. If the cylinders are warmed and sufficient time of aspiration allowed, these two methods will give identical answers.

<sup>1</sup> In this table the macro-urease data represent regular routine work of the laboratory, these and the Benedict data having been obtained by Mr. Bogen. The micro determinations were made by Miss Coleman on the same samples at a much later date. The samples are of urine and represent 100 c.c. in each case. Rose.

## FASTING STUDIES

### 14. The elimination of urinary indican during two fasts of over one hundred days each

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INTRODUCTION. Such fasting experiments as entailed the determination of indican in the urine were reviewed by us in a previous article (1). Comparatively few such experiments have been conducted.

The series of tests reported in this paper were made upon the fasting dog Oscar (2). The fasts were 117 and 105 days in length, respectively. A description of the diet previous to the fast of 117 days, and a general discussion of that experiment, will be found elsewhere (2). The 105 day fast was conducted in a manner similar to the 117 day fast. The conditions differed only in the fact that the 105 day fast was a "repeated" fast (3). The indican method employed was Maillard's modification of Ellinger's method (4), as previously described (5).

EXPERIMENTAL AND DISCUSSION. Instead of separately analyzing the urine of each day of the fast, composite samples, representing different intervals, were prepared and analyzed. The data for the fast of 117 days are given in Table 1 whereas Table 2 contains the data for the fast of 105 days.<sup>1</sup>

The data indicate that there was intestinal putrefaction throughout the fast of 117 days. This is an interesting finding in view of Müller's (6) failure to find any indican in the urine of the professional faster Cetti after the third day of the fast. In previous

<sup>1</sup> On the sixty-first day of the 117 day fast, 100 c.c. of the urine were evaporated to 50 c.c. and the concentrated solution analyzed. Again on the sixty-second and sixty-third days 150 c.c. of each day's sample were taken and evaporated to 50 c.c. before analysis.



fasting experiments made by us on men (1) we have observed that the urine contained indican throughout the course of the fast. Inasmuch as the indican has its origin in protein material one would naturally expect to find it (indican) excreted even during prolonged fasting, since protein material in the form of secretions must be continually passed into the intestine.

Following the period in which the water ingestion of the dog was decreased from 2100 c.c. to 700 c.c. per day, the indican values were higher for several days than they had been during the period of excessive water ingestion. In other experiments a similar decrease in water ingestion has also produced an increased indican output (1, 7).

During the final period of the experiment (64-117 days) the indican output tended to decrease until the 104th day. At this point a rise occurred, which was maintained for several days. The amount of indican excreted on the final day of the experiment (27.3 mg.) was greater than it had been for 50 days, *i. e.*, after the 67th day of the fast. The animal at this time was very weak, and the feces were little more than masses of hair and gave but slight indication of unabsorbed protein material. Perhaps this pronounced increase in indican on the 117th day may be considered as an index of bodily breakdown. According to Maillard (4) an excessive excretion of indican usually accompanies a strained physical or mental condition.

Table 2 embraces the data for the repeated fast of 105 days. The data incorporated there indicate clearly that the indican output was remarkably lowered during the second or "repeated" fast of 105 days.

The differences between the data for the two fasts stand out all the more prominently when it is appreciated that the body weight of the animal was practically the same at the start of each fast and, furthermore, that the diet preparatory to the start of the fasts was similar in the two cases.

The most noteworthy point regarding the data is the absence of all signs of indican in the urine after the 57th day of the "repeated" fast. The processes of intestinal putrefaction therefore underwent a very remarkable decrease as the result of "repeated fasting."

This observation is right in line with previous observations made in our laboratory in connection with repeated fasting. These observations demonstrated increased resistance; a less rapid loss in body weight; a lowering of protein catabolism; and a general physical and mental improvement (3, 8).

TABLE I

*Data pertaining to a fast of 117 days duration*

Days	Average daily urine volume in c.c.	Potassium permanganate solution used in titrating 40 c.c. of clarified sample	Total potassium permanganate solution used for 24 hr. average urine volume	Indican output per day expressed in mg.
Normal period (6 days): 700 c.c. of water per day				
5-7	914	3.40	84.82	22.3
9-11	810	4.20	92.91	24.4
Average	862	3.80	88.86	23.4
Fasting period (117 days): 700 c.c. of water per day				
1-4	554	6.70	101.38	26.6
5-8	493	3.30	46.01	12.1
30-33	517	5.05	71.35	18.7
36-37	544	2.90	43.10	11.3
54-55	493	2.10	28.24	7.4
56-57	505	1.95	26.11	6.9
58-59	475	2.00	25.93	6.8
Average	511	3.43	48.87	12.8
Water ingestion: 2,100 c.c. per day				
60	1385	1.25	47.64	12.4
61	2390	1.45	47.56	12.4
62	1685	3.75	57.96	15.2
63	1840	2.20	35.36	9.3
Average	1825	2.16	47.13	12.3
Water ingestion: 700 c.c. per day				
64	820	8.50	190.24	50.0
65	640	7.05	120.96	31.8
66	545	5.25	77.94	20.5
67	625	6.40	109.71	28.9
80-82	492	5.15	72.70	19.1
92-95	561	3.20	49.03	12.9
104-107	539	3.78	55.51	14.6
115	514	5.20	72.98	19.2
116	550	4.85	66.60	17.5
117	596	7.00	103.83	27.3
Average	588	5.64	91.95	24.2

**SUMMARY.** The course of intestinal putrefaction, as measured by the urinary indican excretion, was followed in two experiments upon the fasting dog Oscar. The initial fast was one of 117 days in length, and the indican output was continuous and fairly high

throughout. The "repeated" fast was 105 days in length, during which the indican values were much lower than during the initial fast. There was an absolute absence of indican in all urine passed during the last 48 days of the "repeated" fast, *i. e.*, after the 57th fasting day. The finding of diminished intestinal putrefaction as a result of "repeated" fasting is in line with other observations from our laboratory which have shown that "repeated fasting" is accompanied by greater resistance; a less rapid loss in body weight; less pronounced protein catabolism; a general physical and mental improvement.

TABLE 2  
*Data pertaining to a fast of 105 days duration*

Days	Average daily urine volume in c.c.	Potassium permanganate solution used in titrating 40 c.c. of clarified sample	Total potassium permanganate solution used for 24 hr. average urine volume	Indican output per day expressed in mg.
Normal pre-fasting period (4 days): 700 c.c. of water ingested per day				
1-4	504	3.26	45.2	11.9
Fasting period (105 days): 700 c.c. of water ingested per day				
1-4	596	4.10	66.8	17.6
5-8	448	3.20	39.2	10.3
26-29	595	2.45	39.7	10.4
42-45	509	2.60	36.1	9.5
54-57	619	1.10	18.7	4.9
66-69	563	0.00	0.0	0.0
78-81	603	0.00	0.0	0.0
90-93	613	0.00	0.0	0.0
102-105	438	0.00	0.0	0.0

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## STUDIES IN WATER DRINKING

### 20. The relationship of water to certain life processes and more especially to nutrition<sup>1</sup>

P. B. HAWK

Many things which are simple and by themselves relatively unimportant, and perhaps of everyday occurrence, are nevertheless of vast importance when considered in connection with related things, events or activities. Although seemingly unessential they are, in fact, vital to securing the desired result. Only by the actual elimination of these things from the course of events does their real value become apparent. The tiny screw is as essential to the efficiency of the mighty mechanism as is the majestic flywheel; the few drops of acid are indispensable for the proper carrying out of the chemical process even though the few drops emerge unchanged from the procedure.

The phrases "free as water," "cheap as water" and "nothing but water to drink" are household phrases and serve to indicate the unappreciative mental attitude of the popular mind toward the vast commercial, agricultural, scientific, medical, and ethical associations which water possesses. The mere enumeration, without discussion, of the important relationships of water would constitute a treatise in itself. In my discussion of the relationships of water I shall limit myself to the consideration of such as are closely associated with certain of the life processes in the animal body and more especially in the human body.

There is generally a good logical basis for any act of nature. Therefore, when we learn by chemical analysis that the human body contains water we at once conclude that water is essential to proper function. However, when we know that water is not only present but that it actually constitutes about two-thirds of the weight of the body, and that a 300-pound man contains only 100 pounds of solid substance, we begin to realize that water must pos-

<sup>1</sup> Read before the American Philosophical Society, Philadelphia, Feb. 6, 1914.

sess associations of which we were not aware or which are so self-evident as to have escaped emphasis.

It is rather startling when we appreciate that the *muscle* which performs such large amounts of physical work is 75 per cent. water; that the *brain* which, in the fulfilment of its function as business manager of the body, correlates and regulates such a vast array of intricate processes and activities, is from 85 to 90 per cent. water; that the *blood* upon which the proper nourishment of every organ and tissue of the body depends is over 90 per cent. water; that the *liver cell* which possesses the ability to initiate or to bring to a successful issue a large number of different processes which are vital to the proper sequence of the metabolic regime is 75 per cent. water; that the *bone*, the tensile strength of which may be 25,000 pounds per square inch, a tensile strength more than twice that of good timber and one and one-fourth times as great as the tensile strength of cast iron, may contain over 40 per cent. of water; and finally, that the *saliva*—the digestive fluid which is able to attack the complex insoluble starch molecules submitted to it in cereals, vegetables, etc., and to reduce them through a large number of definite stages until there finally emerges the soluble maltose which is later made available for purposes of nutrition—contains 99.5 per cent. of water and that its digestive efficiency is further enhanced by increasing its water content. This enumeration of the contents of water in the various tissues and secretions of the body, and the correlation of these values with the important rôle played by these tissues and secretions in the animal economy, emphasizes at once the fact that *water is an extremely essential body constituent*.

Notwithstanding the fact that chemical analysis shows water to be present in every tissue, organ, cell, secretion and fluid of the body, one may imagine that such an inoffensive and apparently unimportant substance as water cannot coöperate in any *material* way in the successful carrying out of the multitudinous important functions of the body. This idea is quickly dispelled, however, if we eliminate water from our dietary for even a short interval of time. Under such conditions every important function of the body, whether based upon physical, chemical or psychical foundation, is lowered in its efficiency. This lowered efficiency is not so evident when one abstains



from food, but drinks plenty of water. In fact the mental faculties may be sharpened by a short fast. This point was clearly shown in one of our fasting tests. A member of the chemical staff, a candidate for the Ph.D. degree, was the subject of the test. During a seven-day fast he worked hard in preparation for his final examinations and *ingested nothing but water*. He subsequently stated that he felt he had accomplished more work, mentally, during the seven days of the fast than in any other period of equal length during his entire course. This observation is in sharp contrast with another observation made by my associates and myself. In this case we were to study the influence of an *increased* water consumption. In order that a pronounced difference in the volume of water ingested in the different experimental periods might be secured, the amount of water given the subjects of the experiment (men) during the preliminary period was reduced to a minimum. That we had exceeded the physiological minimum was soon apparent; headaches, nervousness, loss of appetite, digestive disturbances and inability to do accurate chemical work were evident. It was necessary, therefore, to *increase the water content of the diet*, and with this single change the experiment proceeded satisfactorily. The incidents just mentioned serve to emphasize the fact that *one may live longer without food than without water*.

It is also a demonstrated fact that the length of time an animal is able to fast will be considerably increased if it be given a uniform volume of water daily instead of being subjected to a "complete" fast, *i. e.*, without food or water. This fact was emphasized in one of our experiments in which a Scotch collie dog fasted for periods of 117 and 105 days respectively in successive years, the animal having been given a uniform volume of water daily by means of a stomach tube.

The vast majority of the processes and activities associated with the digestion and absorption of our food, the utilization of the digestion products as a source of energy and for constructive purposes, as well as the transformations associated with the excretion of waste products, are at basis *chemical*. These chemical reactions take place *only in solution*. A solvent is necessary; the best, most available and least injurious is water. When we turn to respiration

here again we are confronted by chemical and physical processes which are dependent upon the presence of water. In the first place the surface of the lungs must be moist before there can be any exchange of carbon dioxide and oxygen by diffusion; and secondly, the blood cells are transported in a fluid medium. The regulation of the temperature of the body is facilitated by the presence of circulating water and the evaporation of water from the surface of the skin. Water serves as a medium by which nutritive material is carried to the body cells. All mucous surfaces of the human body require the presence of water before they can function normally; a dry mucous membrane is unable to play the rôle for which it was designed. Water also has an important relationship to absorption. If the end-products of digestion in the intestine are not present in proper dilution they will not be most efficiently absorbed. It has been shown by experiment that *dilute* solutions of sugar (glucose), for example, are absorbed much more satisfactorily from the intestine than are concentrated solutions. If the sugar is present in higher concentration than 8 per cent. a diluting secretion emerges from the walls of the intestine to bring about proper dilution. Moreover, the elimination of toxic substances from the body is accomplished more satisfactorily if they are brought to the kidney well diluted.

In addition to the above classes of activities, which are made possible or facilitated by the presence of water, there are many other chemical processes in the human body which not only require water for their proper conduct, but which are accompanied by the loss or gain of water to the chemical structures undergoing change. I refer to the changes which are accompanied by hydrolysis and dehydrolysis or anhydrolysis. A reaction of this character occurs when our physician prescribes ammonium benzoate. In the body this ammonium benzoate is split into benzoic acid and ammonia. The kidney then takes the benzoic acid and conjugates it with glycocoll, the synthesis being accompanied by the *liberation of water* and the formation of hippuric acid, which is excreted in the urine. In poisoning by methyl alcohol, the alcohol is oxidized in the body to formic acid and *water*. When phenolphthalein is used as a cathartic it comes in contact with the sodium carbonate in the intestine, *water*

is split off and the sodium salt of phenolphthalein results. This sodium salt then exerts its irritant action and purgation ensues. Consider the complex organic molecule we call lecithin: it occurs in animal and vegetable cells; is present as an important constituent of brain and nerve tissue, in addition to being present in varying proportions in many of the fluids and secretions of the human body; and has been said to be related importantly to the problem of growth. One of the lecithins, the so-called *di-stearyl lecithin*, bears the formula  $C_{44}H_{90}NPO_9$ , which shows it possesses a complex structure. Yet water easily reduces it to its lowest terms. In other words the addition of 4 molecules of water causes this complex lecithin molecule to disintegrate; and we have, as fragments, 2 molecules of stearic acid, and one molecule each of glycerol, cholin and phosphoric acid. Water was the magic key which unlocked the complex lecithin molecule and enabled us to read its internal structure.

In other chemical connections water is the *keystone of the molecular arch*, and its removal is accompanied by the destruction of the molecule.

A good illustration of many of the important relationships of water is afforded by the life history of protein, from its ingestion to the excretion of its waste residues. We know that proteins are absolutely essential to the proper nourishment of the human body. In practically all forms in which they are ingested by man they contain *water*. When they reach the stomach they come in contact with the gastric juice which is 98 per cent. *water*. They are there acted on by pepsin, a proteolytic enzyme which causes the protein molecule to *take on water* and break down into substances of a simpler structure than the original protein. These protein cleavage products are then carried into the intestine where the acid of the gastric juice is neutralized by the sodium carbonate present in the aqueous solution we term the pancreatic juice, *water* being formed in the process of neutralization. The enzyme trypsin of the alkaline pancreatic secretion then acts upon the protein cleavage products, *adds water* to their structure and splits them into still simpler substances. The intestinal juice, which is 98 per cent. *water* now lends its assistance and the enzyme erepsin of this secretion aids by a *hydrolytic process* in the production of the final cleavage prod-

ucts, the amino acids. These crystalline acids with the help of *water* now pass through the walls of the intestine into the blood, which is over 90 per cent. *water*. Borne along by the blood stream these amino acids are quickly transported to the various tissues and organs of the body. Such of the acids as are needed for cell construction are linked together to form the basis of new cell protein, *water* being a by-product of the synthesis. Such of the amino acids as are not needed for this purpose are shorn of their nitrogen by a deamination procedure, the amino acid being thus split into two portions, one nitrogenous, the other carbonaceous. The ammonia formed from the nitrogenous part is passed into the blood where in the presence of carbonic acid ammonium carbonate is formed. By the removal of *water* from this carbonate we obtain the corresponding carbamate and, by the *removal of water* from the carbamate, urea results. The urea is then removed from the blood by the kidneys and excreted in an *aqueous* solution, the urine. In the meantime the carbonaceous portion of the amino acid has been oxidized in the tissues to yield energy, *water* and carbon dioxide being the final products of this combustion.

The varied relationships of water that are associated with the proper digestion, absorption, metabolism and excretion of protein are present, although in a somewhat less accentuated degree, in the cases of fats and carbohydrates. In other words, *the digestive and metabolic transformation of all essential food stuffs is inseparably and vitally associated with water*. The changes being essentially chemical, they require the presence of water before they can be carried to successful completion; and the actual processes themselves are almost universally accompanied by a definite change in chemical structure that is associated with the gain or loss of water to the molecule. For example, when we ingest sucrose (cane sugar) we are ingesting a very soluble and easily diffusible substance. In spite of these physical characteristics it is not available for the uses of the organism because of its chemical structure. If this cane sugar molecule,  $C_{12}H_{22}O_{11}$ , be introduced into the human body by any means other than the gastro-intestinal tract it is excreted in the urine unchanged except for a certain percentage (35 per cent.), which Abderhalden would have us believe is transformed in the body under



the influence of a defensive enzyme and made available for the uses of the organism. The conditions are entirely different when the cane sugar is *ingested*. In this event the carbohydrate proceeds essentially unaltered until it reaches the intestinal juice, where, through the instrumentality of the inverting enzyme invertase, or *sucrase*, a *molecule of water* is added to the disaccharide molecule, causing the  $C_{12}H_{22}O_{11}$  to split into two monosaccharide molecules, which are absorbed and utilized by the body. The addition of the tiny molecule of water ( $H_2O$ ) has yielded a 100 per cent. nutritional efficiency from the nutritionally inefficient cane sugar.

Many important experiments have been made to demonstrate the influence of an *increased water ingestion* upon the processes of metabolism. Inasmuch as protein is a very important dietary constituent the main emphasis in these tests has been placed upon the metabolism of protein. These experiments show that an increased consumption of water is followed by an increased output of nitrogen in the urine. As to the history of this nitrogen there is a difference of opinion, and two hypotheses have been suggested. Some investigators tell us that the increased nitrogen is due to the "flushing" of the tissues and the consequent removal of nitrogenous waste products which had accumulated there. Other investigators tell us that the increased nitrogen has its origin in an increased protein catabolism. The first really definite evidence favoring either of these views was furnished by certain of our experiments. It is well known that all cells contain nucleoprotein. By decomposition this nucleoprotein yields purin bases and uric acid. In certain lower animals, in particular, oxidation of uric acid may yield allantoin. The nitrogen in the form of purin bases, uric acid, and allantoin is termed "total purin nitrogen." Inasmuch as this form of nitrogen has its origin in the cell nucleus we may consider that an increased output indicates stimulated cellular activity and increased tissue disintegration. In one of our tests a dog was fasted 59 days, receiving 700 cc. of water daily. The water ingestion was then increased 200 per cent. for four days, making the water ingestion 2100 cc. per day. Under these conditions an increased output of total purin nitrogen was observed. This increased excretion of purin nitrogen, which followed the increase in the water ingestion to 2100 cc. per



day, must have been due to the stimulation of the catabolism of cellular material, since it is apparent that the tissues of the animal must have been thoroughly "flushed" during the previous ingestion of 700 cc. of water daily for an interval of 59 days.

Certain others of our experiments also favor the view that water stimulates tissue changes. Muscular tissue contains creatin. Normal urine does not contain creatin. If a normal person drinks a large volume of water the urine of that person contains creatin. This observation has been made repeatedly in our studies and has been interpreted as indicating the disintegration of muscular tissue and the excretion of its contained creatin in the urine.

The medical men of to-day appreciate fully the immense importance of water to the human body. The great development along hydrotherapeutic lines attests this fact. However, pursuant to a tradition of long standing the great majority of physicians advise against the drinking of water *at meal-time*. In fact the diet lists of stomach specialists frequently bear a printed admonition to "take no more than one and one-half glasses of fluid at any meal." The following quotation indicates in a general way the attitude of the average physician toward the drinking of water with meals: "We can lay down the definite and certain rule that water should never be drunk at meals, and preferably not for at least one hour after the meal is eaten. The effect of drinking water while eating is, first, to artificially moisten the food, thus hindering the normal and healthful flow of saliva and the other digestive juices; secondly, to dilute the various juices to an abnormal extent; and, thirdly, to wash the food elements through the stomach and into the intestine before they have had time to become thoroughly liquified and digested. The effects of this upon the welfare of the whole organism can only be described as direful."

As a matter of fact not one of the statements in the foregoing quotation has any experimental basis. We ourselves have demonstrated that saliva acts more efficiently when diluted with seven volumes of water. Experiments have also demonstrated that the entrance of water into the stomach *stimulates* the flow of gastric juice. Not only this but the juice as secreted has a higher acid concentration than that secreted previous to the entrance of the water.

After stimulating the gastric secretion the main bulk of the water very quickly enters the intestine, but it does not carry with it any appreciable part of the solids present in the stomach.

An abstract in a recent number of the *Journal of the American Medical Association* (Jan. 31) quotes a French worker as claiming that water may leave the *empty* stomach very quickly but that it may *remain for hours if the stomach contains food*. This statement is rather at variance with Cohnheim's demonstration, by means of bismuth feeding and X-ray examination, that water leaves the full stomach very quickly by means of a trough along the lesser curvature.

My associates and myself have made a large number of experiments upon the influence of water drinking with meals. Men and lower animals have been used as subjects. When we initiated our experiments upon man we were unable at first to get suitable subjects. The deep seated prejudice against the drinking of water at mealtime, and the mental vision of the direful results to follow acted as a barrier against which our inducements were of no avail. At length, however, a member of the staff of our department announced that he was ready to "take a chance" as he expressed it. From the *psychical* standpoint, therefore, everything was against the water. I shall summarize briefly what the water was able to do, in spite of the psychical handicap, in this first experiment and in others of a similar character which followed.

First, just a word as to the character of the diet employed and the experimental plan followed. In all cases both diet and experimental plan were very simple. The diet consisted of graham crackers, butter, milk, peanut butter and water. Uniform quantities of these dietary constituents were ingested by the subject of the experiment for a period of about one week, this interval constituting what we termed our *preliminary* or *normal* period. The excreta for each day were collected and analyzed and the data thus secured constituted our normal basis for comparison. Next came our true *experimental* period or *water* period as we called it. During this period the diet was the same as during the preliminary period except that *the subject was required to drink at each meal a volume of water ranging from 500 cc. to 1300 cc. in excess of that previously taken*.

This period was generally from 5 to 10 days in length. At the end of the period the diet, as fed during the *preliminary* period, was again resumed for about one week, this interval constituting our *final* or *after* period. This experimental plan gave us an interval of so-called excessive water ingestion preceded and followed by periods during which so-called *normal* quantities of water were daily ingested.

So far as the influence of water upon the flow and activity of the digestive secretions is concerned, we have demonstrated in the first place, by experiments *in vitro*, that the digestive efficiency of the salivary secretion as before mentioned is increased by dilution with water, the optimum dilution being *seven volumes*. We have also verified, in an indirect way, the observation that water stimulates the flow of gastric juice.<sup>2</sup> Our index was the ammonia content of the urine. We observed that an increased water consumption was accompanied by an increase in the amount of ammonia in the urine and that, for any given individual, a pronounced increase in the water ingestion generally produced a correspondingly pronounced increase in the ammonia output, whereas a smaller increase in the water ingestion was accompanied by a proportionate increase in the output of ammonia. Now, the ingestion of dilute mineral acid solutions by man or lower animals has also been shown to cause an increase in the urinary ammonia. Furthermore, tests by several investigators upon dogs with a portion of the stomach isolated in the form of a so-called Pavlov pouch or Pavlov stomach, have demonstrated that the entrance of water into the stomach is accompanied by *an increased flow of gastric juice*. Not only is the volume of juice increased, but the acidity of the juice as well. This being true, the ingestion of water must of necessity cause the passage into the intestine of an *increased quantity of hydrochloric acid from the gastric secretion*. Therefore, in view of the fact that acid ingestion, or the normal or pathological production of acid in the body, is accompanied by an increased ammonia excretion, we interpret the heightened ammonia output observed by us in our water studies as due to the stimulation of the gastric function.

<sup>2</sup> Since this paper was read the author in collaboration with Dr. M. E. Rehfuess and Dr. Olaf Bergeim has demonstrated the stimulating power of water in a *direct* way upon the human stomach. (*Jour. Am. Med. Assn.*, 63, 909, 1914.)

So far as the pancreatic secretion is concerned certain of our experiments indicate that the ingestion of large volumes of water at mealtime stimulates the pancreatic function indirectly through the entrance of the increased volume of acid chyme into the duodenum.

In view of the stimulated salivary, gastric and pancreatic functions, and the more efficient activity of the digestive enzymes contained in these secretions, one would naturally expect that the ingested food would be more completely utilized by the human body under the influence of an abundant water intake. A better utilization of the three nutrients—protein, fat, and carbohydrate—has been demonstrated in our experiments. If the food is better utilized, then a smaller quota of unabsorbed residues of food and secretions will remain in the intestine to form media for the growth of bacteria. In several of our experiments quantitative determinations of these bacteria were made and in every case water drinking with meals was accompanied by a decreased growth of microorganisms; and, associated with this decreased bacterial development, occurred a decrease in the processes of intestinal putrefaction. The increased flow of acid chyme into the intestine also militates against the activity of the putrefactive bacteria, inasmuch as such microorganisms do not thrive in an acid medium.

Our experiments just summarized indicate that the drinking of water with meals exerts a desirable influence upon a number of the most important of the activities and functions of the gastro-intestinal tract. I have considered these activities in logical order beginning with the oral cavity and ending with the large intestine. Our experiments were not made in this order, however, our first study being concerned with the development of intestinal bacteria whereas one of our most recent tests was concerned with the activity of the salivary secretion.

The water used in all of our experiments thus far mentioned was *softened* water. This was prepared by treating ordinary city water with one-sixth its volume of saturated lime-water and filtering off the resultant precipitate. Having established various beneficial relationships for softened water the question arose as to whether the drinking of *distilled* water at mealtime would have a similar influence. A belief very widely held by both the laity and the scientific



worker is to the effect that the ingestion of distilled water is a bad procedure. The absence of inorganic matter in such water is believed to be the forerunner of various untoward influences upon the processes of digestion and absorption. So far as I am aware there is no experimental basis for such a belief. An eminent English scientist has written as follows concerning the influence of distilled water: "If tissues or cells are placed in distilled water, passage of water into the cells occurs owing to the difference of osmotic pressure. The cells swell up and may finally burst and die. A similar poisonous action on cells is observed when distilled water is drunk. In this case the surface layers of the epithelium of the stomach undergo considerable swelling; salts also pass out and the cells may die and be cast off. This may lead to catarrh of the stomach."

If this eminent scientist's claims are true then one of our fasting tests is a notable exception. This is the fast which continued for over 100 days and to which reference has already been made. The fasting dog was given 700 cc. of distilled water daily by means of a stomach tube, and yet at the end of the fast the post-mortem examination failed to show any evidence of a deranged gastric mucosa. Certainly a period of over 100 days is a sufficiently long interval in which to demonstrate the toxic influence of distilled water if such an influence is demonstrable. Particularly is this true of the fasting animal, which may possess a lowered resistance to toxic influences.

However, if we grant that distilled water, because of the absence of electrolytes, does possess a pernicious influence upon the gastric mucosa, it is quite logical to believe that such influence will be exerted to the maximum by distilled water taken *between meals*. Because of the electrolyte content of the average diet distilled water taken along with such a diet will cease to act as distilled water soon after it reaches the stomach. The toxic action of distilled water, if such action is demonstrable, must be more in evidence when the distilled water passes into the relatively *empty* stomach. So far as the swelling and ultimate bursting of the cells under the influence of osmotic forces is concerned, it must be apparent that osmotic phenomena which are exhibited by non-living, excised cells do not necessarily hold for cells actually functioning in the animal body.



Distilled water in contact with a cell of the living body may through osmotic influence, cause a swelling of the cell, but the actual bursting of the cell will of course be prevented by physiological factors which will be called into play, thus causing the circulation to remove the excess fluid.

Various clinical views have been expressed as to the influence of distilled-water ingestion. Some clinicians claim to have found it harmful in certain instances, others claim it is harmless, while still others express the opinion that the question as to its harmfulness or harmlessness must be considered an open one. The catarrhal conditions which have been found to follow the drinking of water from glaciers, or the excessive ingestion of ice, may possibly have had their origin in the low temperature rather than in the absence of electrolytes.

In our own experiments upon the influence of distilled-water ingestion with meals, we were able to demonstrate a stimulation of the gastric and pancreatic functions, better digestion and absorption of ingested food, a decrease in the growth of intestinal bacteria, and a lessening of putrefactive processes in the intestine.

A foreign investigator has recently claimed that distilled-water ingestion by white mice causes hemoglobinuria. It is well known that the introduction of distilled water *into the circulation* will produce a transient hemoglobinuria. I fail to see, however, how the introduction of distilled water *into the stomach* can bring about hemoglobinuria.

A word regarding mineral waters. I have expressed a belief that distilled water is efficient although it contains no electrolytes. I also believe that many mineral waters, when ingested, owe their therapeutic efficiency not to their contained electrolytes but rather to the volume of water consumed. This argument does not hold for radio-active waters nor for waters which are taken because of their cathartic action.

The scientific inaccuracy of the lithia treatment in certain disorders is well known. Hare speaks as follows regarding the therapeutic value of lithia water in *gout* and *rheumatoid arthritis*:—"Although lithium forms salts with uric acid in the test-tube, in the body it has a greater affinity for the acid sodium phosphate in the

blood, and practically leaves the uric acid to itself. This is an important point, since it proves that *the large amount of water generally taken with lithium salts has more to do with relieving gout than has the lithia.*"

Before closing I would like to emphasize the fact that, in all of the water studies made by my associates and myself, *normal* subjects have been employed. We have made no clinical studies and have made no clinical suggestions. It is probably true that a person with a deranged circulatory or gastric function, or any pronounced lesion of heart or kidney, should not drink large volumes of water at *any time*, either with meals or between meals. The ingestion of large volumes of water with meals is probably contraindicated in *atonic* or *dilated stomach*, since an excessive water ingestion might promote further atony and dilation. It is also probably contraindicated in gastropnoia, where the gastric support is relaxed and insufficient and in certain cases of pyloric colic or spasm. If contraindicated in these conditions, however, it is because a large volume or weight at any one time is contraindicated and *not because of the water per se*. I would say, therefore, that *normal* persons may drink freely, of *water*, at mealtime, whereas those unfortunate individuals who possess lesions of heart or kidney or who are troubled with any circulatory or gastric disturbance, should have their fluid intake regulated strictly according to medical advice.

On the basis of a large number of experiments we feel warranted in concluding that the average normal individual will find that *the drinking of a reasonable volume of water with meals will promote the secretion and activity of the digestive juices, the digestion and absorption of the ingested food, and will retard the growth of intestinal bacteria and lessen the extent of the putrefaction processes in the intestine.*

Our claims for the efficiency of water have been verified by Bradley, who found that pancreatic lipase acted more satisfactorily when its solution was diluted with water; by Smirnov, who demonstrated that fasting rabbits which were permitted free access to water were less prone to show signs of fatty infiltration of the liver than were similar fasting rabbits which were not permitted to drink water; by Niles, who made an experiment upon sixteen medical students and

demonstrated that the drinking of one quart of water with each meal for a period of one week failed to produce "a single qualm of indigestion, either gastric or intestinal." Our claims are supported by the habits of our aboriginal forefathers, who "lugged their food down to the bank of the stream and facilitated the feeding process by copious gulps of water"; of the *captive bird*, whose dietary procedure embraces the alternate ingestion of tiny seed and water drop; of the *baby* at the mother's breast, who is so satisfactorily nourished by a food which is 87 per cent. water; of a large number of *physicians*, who have always ingested considerable water with meals, although forced by a popular delusion to admonish their patients otherwise; and, finally, of a vast multitude of the *laity*, who have habitually taken water with their meals, in spite of the admonition of the family physician, and who to-day bear testimony to the efficiency of the practice, in their freedom from digestive disturbances, or who have finally died from old age or from some disorder entirely unrelated to water ingestion.

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## MUSCULAR WORK AND THE RESPIRATORY QUOTIENT

SERGIUS MORGULIS

All investigations of the physiology of muscular work aim at a solution of two fundamental problems: the organism's mechanical efficiency and the source of the energy of the working muscle. One is a problem in animal calorimetry; the other, in metabolism of matter. Since the respiratory quotient, or ratio between the carbon dioxid exhaled and the oxygen consumed, indicates the nature of the material oxidized in the organism, the gaseous metabolism offers the best means of determining the source of energy in muscular work.

Chauveau, on the basis of his experiments (which unfortunately have never been described in detail and in which the respiratory quotient was observed to increase from 0.75 to 0.95 during strenuous exercise), advanced the hypothesis that glycogen is the source of muscular energy. To account for all the facts, Chauveau was obliged to postulate further that, as the glycogen is consumed, new quantities are supplied to the muscles, such added quantities being formed from fat by direct chemical change. This hypothesis met Prof. N. Zuntz's sharp criticism on theoretical as well as experimental grounds. First, the high respiratory quotient in Chauveau's experiments is obtained at a stage, of the exhausting work, which is so far advanced that it is reasonable to believe that by that time the glycogen would be entirely used up. Furthermore, a transformation of fat into glycogen sufficiently to supply the necessary energy for muscular contraction would be a physiologically wasteful process, as nearly a third of the potential energy would thereby be lost to the organism.

Unlike Chauveau, Prof. Zuntz and his students in their numerous researches found the same respiratory quotient before and during work. In one of the last issues of Oppenheimer's *Handbuch*

*der Biochemie*, Prof. Zuntz defends the thesis that all body materials can yield energy to the working muscle.

The Carnegie Institution of Washington recently published a monograph by F. G. Benedict and E. P. Cathcart,<sup>1</sup> dealing with the metabolism of muscular work, which is of the utmost interest as a very noteworthy contribution to an acutely debated subject. Besides, the scientific reputation of its authors, the perfection of the apparatus for measuring the external work, and the unsurpassed resources of the Carnegie Institution for experimental investigation, vouch for the importance of the monograph.

This monograph appears to offer substantial support to Chauveau's hypothesis. In practically all the work-experiments, the respiratory quotient increased, attaining especially high values in severe work. Respiratory quotients of 1.00, indicating pure carbohydrate consumption, were not infrequent and in a number of experiments it was even greater than 1.00. This last fact which, if correct, implies a transformation of glycogen into fat as a result of severe work, is so incredible that it seems necessary to assume that some serious source of experimental error has been overlooked. A scrutiny of the technic shows that this assumption is justified.

The very high respiratory quotients were usually coincident with rapid breathing on the part of the subject. Thus, in one series of experiments, as the resistance was gradually increased, the rate of respiration per min. changed from 18-22 to 36-40, while the respiratory quotient also changed from 0.87 to 1.00. In another set of work-experiments, the respiratory quotient was 0.80-0.83 during light exertion, when the rate of respiration was 20-24 but, as the work became more severe, the respiratory quotient increased to 0.97-1.03 and the respiration rate became 36-38 per min. We know, of course, that both carbon dioxid and water vapor are given off through the lungs and, under forced breathing, their absolute quantities increase greatly. In the two sets of experiments just referred to, the carbon dioxid elimination increased 2 to 2.5 times and exceeded 2.5 liters per min. No determination was made of the amount of water expired during the same time but the quantity must likewise have been much greater. Is it not possible that some

<sup>1</sup> Benedict and Cathcart: *Muscular work; a metabolic study with special reference to the efficiency of the human body as a machine*. Pp. 176, 1913.



of that water was weighed as carbon dioxid, thus giving an erroneously large value to the latter and making, therefore, the quotients appear very high?

To clarify the above reasoning, and to substantiate it, a brief diversion will be made to point out the essential features of the technic. The subject, riding a bicycle ergometer, breathed through a closely connected series of bottles, some of which contained soda-lime for the absorption of carbon dioxid, and others contained sulfuric acid for the absorption of water. The produced carbon dioxid was determined directly by weighing the soda-lime bottles before and immediately after the experiment. Oxygen was supplied from a cylinder and was also measured by weight.

Since soda-lime takes up water as well as carbon dioxid, it was the most important object of the technic to rid the air of absolutely every trace of moisture before it passed through the weighed absorber. Two large sulfuric acid wash-bottles were placed in the circuit for this purpose. It is obvious that any failure of these wash-bottles to hold the moisture in the expired air must have resulted in an accumulation of water in the soda-lime and, adding to its weight, caused a rise in the quotient. Much as this particular part of the apparatus requires constant attention, therefore, it seems nevertheless to have been seriously neglected by the authors of the monograph. At any rate, in the lengthy discussion of the various possibilities of error and of the careful manner in which these possibilities were precluded, no allusion is made to this matter.

Examining the picture of the apparatus, on the front page of the monograph, as well as the diagram in the text, it is evident that not only was the air-drying portion sadly neglected but also its arrangement was such as *to favor the escape of moisture into the soda-lime*. The ingoing tube, as is seen there, extends but a short distance below the surface of the acid and permits the strong current of air to pass speedily through a very small amount of acid, the period of contact between the two being very brief. Considering that the gaseous exchange during work is probably tenfold that during rest, the rate of ventilation must have been very rapid to free the system of the large quantities of resultant carbon dioxid. There is no direct information on that point but, if we assume that at least 600 liters of

air passed through the sulfuric acid wash-bottle in the course of a work-experiment usually lasting ten minutes, the conditions were most unfavorable for the complete removal of moisture from the expired air.

The accuracy of the carbon dioxid determination by the Fresenius method depends largely on careful regulation of the air current, and every means is employed in that method to increase the surface of contact between the air and the sulfuric acid. In Atwater's respiration calorimeter, likewise, the large jars used for drying the air have a special internal construction that increases and prolongs the absorbing action of the sulfuric acid on the moist air. It is highly improbable that a current of air, especially when saturated with moisture, could be freed from all its water while merely striking a superficial layer of acid at a speed of at least one liter per second. All experience points against that. The results of the carbon dioxid determinations relating to the bicycle rider cannot, therefore, be credited unless it could be shown, against all experience, that the air was actually freed from every trace of moisture by the inefficient arrangement employed.

To explain his respiratory quotients Chauveau resorted to the hypothesis that fat is transformed intramolecularly to furnish the exhausted muscle with glycogen. To be consistent in the interpretation of their quotients, which in a few tests under severe work exceeded one, Benedict and Cathcart would have to acknowledge that glycogen is apparently transformed into fat, which is then reconverted into glycogen before it is oxidized in the working muscle.

It is a matter of deep regret that the expectation which the appearance of this monograph inspired, of a definite solution of a very important problem in metabolism, has not been realized. A work of great excellence in the main from a technical viewpoint, it is probably destined to contribute more towards confusing than clarifying the subject of muscular work.

Chauveau's hypothesis failing to receive corroboration from reliable experiments, Prof. Zuntz's alternative theory is the only acceptable one at the present time.

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## ADDENDUM

Since the foregoing was written (March) I have had occasion to install, in the Woods Hole Laboratory of the Bureau of Fisheries, a small apparatus for the determination of carbon dioxid. The work with this apparatus is still in progress and the results will be published later, but I wish to add here a brief account of some of my experience in handling this apparatus, which supports the above criticism of the technic of Benedict and Cathcart's investigation.

When I first put up the apparatus, it seemed quite sufficient, for the *complete* removal of moisture, to bubble the air through two connected wash-bottles containing sulfuric acid, one of which was half-full of glass beads (3 mm. diam.). This seemed specially effective because the ventilation was relatively slow (probably less than one hundredth as rapid as that in the Benedict-Cathcart apparatus) and, although the air was saturated with water vapor, the surface of contact with the absorbent was very extensive.

In the early blank experiments with this apparatus, an increase in weight of the soda-lime and calcium chlorid tubes was observed that was very hard to explain. Various possibilities were tested and at last, as it seemed certain that the increase in weight must have been due to retention of water, a third sulfuric acid wash-bottle was added to the series. The effect was unmistakable, and the increase in weight was at once shifted from the first to the third decimal place. This experience was rather striking and convinced me of the need of very strict control at that point of the apparatus. I therefore inserted between the last sulfuric acid wash-bottle and the soda-lime tubes, a U-tube with glass beads submerged in a little sulfuric acid in the bend. This tube is weighed, now, before and after each experiment; and constancy in its weight is the only guaranty that the accuracy of the technic is not affected from that source.

In spite of the increased labor, the results with this new arrangement and experimental procedure are most gratifying. In later successful blank experiments the change in weight was found to be very insignificant. The improved apparatus can be employed with complete reliance upon the accuracy of the results obtained with it.

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## BLEACHED FLOUR

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Bleached flour is a subject which has engaged the attention of scientists and millers for the past ten or more years, especially in great wheat producing countries like our own. Whether or not the use of bleached flour is injurious has been argued pro and con, but the solution of the problem is still in doubt.

Naturally the question arises, "Why is flour bleached?" The reason is purely a commercial one. For instance, a miller sends out in the fall or spring a salesman with a number of samples of flour which have not been bleached. Orders are taken for the flour and four or five months later, when the delivery is made, the flour has whitened or bleached to an appreciable extent, due to atmospheric conditions. Quite naturally the purchaser objects to accepting the consignment. For this reason the millers have bleached their flour in order to have it always uniform in color.

Up to the last decade the method employed was to store the flour for a period of several months whereby the more or less marked color was removed.

A number of years ago Frichot<sup>1</sup> observed that the gas produced by discharges of electricity through air were capable of whitening the flour. This he attributed to the production of ozone. Some time later the Messrs. Andrews<sup>2</sup> discovered that the bleaching was brought about by the action of certain oxides of nitrogen, which are produced when nitric acid is brought in contact with a reducing agent such as ferrous sulfate.

Numerous processes have been devised for the application of this principle to the practical bleaching of flour. The process which, up to the present time, has proved most serviceable is known as the Alsop process. By this method air is pumped through a chamber

<sup>1</sup> Frichot: French patent, 277751 (1898).

<sup>2</sup> Andrews (J and S): English patent, 1661 (1901).



in which a flaming electric arc is discharging. More recently the use of nitrosyl chlorid has been introduced as a means of bleaching flour, and possesses advantages over the oxid of nitrogen in the character of the bleach which it produces as well as in the simplicity of application to the flour.

Is there any difference chemically between bleached and unbleached flour? Analyses have shown that the chemical composition of both is practically the same, with the exception that in the case of bleached flour nitrite is present, whereas in the unbleached flour, nitrite is absent. Analyses made by me have corroborated this fact, as shown in detail by the following summaries:

Average analytic data:

<i>Unbleached flour.</i>		<i>Bleached flour.</i>	
	Per Cent.		Per Cent.
Nitrogen .....	2.47	Nitrogen .....	2.43
Proteins .....	15.73	Proteins .....	15.48
Fat .....	1.73	Fat .....	1.92
Dry gluten .....	11.60	Dry gluten .....	11.37
Moist gluten .....	29.29	Moist gluten .....	31.02
Phosphate ( $P_2O_5$ ).....	0.508	Phosphate ( $P_2O_5$ ).....	0.598
Nitrite .....	absent	Nitrite .....	present.

The presence of nitrite in flour has led to a great deal of discussion as to whether or not the use of bleached flour is injurious to health. Some investigators claim that the presence of nitrite in flour reduces the oxyhemoglobin of the blood to methemoglobin. In order to prove or disprove this claim we have conducted a number of experiments upon guinea pigs and rabbits in the following manner. Each of six healthy guinea pigs was given, morning and night by mouth, one drop of 1 percent sol. of potassium nitrite, i. e., about 1 mg. of  $KNO_2$ . At the end of three weeks, several drops of blood were obtained from an ear of each guinea pig, mixed with 10 cc. of physiological salt solution, and examinations made with the spectroscope. In every case the blood showed only normal oxyhemoglobin. Spectroscope readings were made at intervals of three days, with negative results.

A modification of the first experiment was begun, six weeks after the first experiment was started, with another set of guinea pigs.



Instead of using one drop of 1 percent sol. of potassium nitrite, five drops (containing 5 mg.) were used. The blood of these guinea pigs was examined spectroscopically, after three weeks' administration of the nitrite sol., and also at intervals of three days, but up to the present time (three months after the experiment was begun), we have been unable to find any deviation from normal in the blood of the guinea pigs that received the small dose, or in the blood of the ones that received the large dose of potassium nitrite sol. During this time two of our guinea pigs died, but autopsies showed no conditions indicative of potassium nitrite poisoning, death apparently resulting from natural causes.

When we started the second series of guinea pig tests, we took two pounds of unbleached flour, put it in a bottle, added two liters of petroleum ether, and shook vigorously on a mechanical shaker for 24 hr. The mixture was then filtered through hard filter paper; the filtrate was greenish-yellow. We then passed peroxide of nitrogen gas (obtained by the action of nitric acid on metallic copper) through the liquid, completely decolorizing it, as well as causing a grayish-white substance to be precipitated, which later, on exposure to air, became brown in color and resinous in appearance. This precipitate was obtained by filtration and washing repeatedly with petroleum ether. A little of this gave a pronounced pink color with Greiss's reagent, showing the presence of nitrite. The precipitate was slightly soluble in water, alcohol and the common solvents.

The Liebermann test for nitrosamines was then made, as follows: A small amount of precipitate was placed in an evaporation dish, several drops of conc. sulfuric, and conc. carbolic, acid added and a greenish-red color obtained which, when diluted with water, gave a red color. The addition of sodium hydroxid to alkalinity caused a bluish-green color, showing the presence of a nitrosamine or secondary amine. It is a question whether nitrite or nitrosamine gives this color reaction.

A rabbit was then fasted for two days and the precipitated nitrosamine, obtained from two pounds of flour in the manner described above, was rubbed up with a little water in a mortar and introduced into the stomach by means of a catheter. The animal

showed no poisonous effect after the administration of the nitrosamine, but gained in weight. A spectroscopic examination of the blood showed no deviation from normal.

Three months after the administration of the nitrite sol. was begun, all the animals were autopsied. The findings showed that all were normal.

The results of these experiments convince us that the use of bleached flour is not detrimental to health. Although nitrite is present, due to the bleaching process, it is not sufficient in quantity to cause the formation of methemoglobin or the replacement of normal oxyhemoglobin. We have found no pathological conditions in our experimental animals arising from the administration of nitrite, even with doses that were much greater than the quantities of nitrite present in the flour.

To Dr. Victor C. Vaughan I wish to express my gratitude for the valuable suggestions and assistance extended to me.

*Department of Chemistry,  
School of Medicine,  
University of Alabama, Mobile.*

MEETINGS OF THE BIOLOGICAL DIVISION OF THE  
AMERICAN CHEMICAL SOCIETY, CINCINNATI,  
OHIO, APRIL 8 AND 9, 1914

PROCEEDINGS REPORTED BY THE SECRETARY,

ISAAC KING PHELPS

At the meetings of the Biolog. Div. of the Amer. Chem. Soc., held at Cincinnati on April 8 and 9, 1914, the papers abstracted below were read and discussed.<sup>1</sup>

**Chemical studies upon the genus *Zygadenus*.** CARL L. ALSBERG. (*Bur. of Plant Industry, U. S. Dep't of Agric.*) A number of species of plants of the genus *Zygadenus* are regarded as poisonous. Great confusion from the toxicological standpoint has existed in this genus because the nomenclature of the genus has not always been clearly understood. Thus the alkaloids of the "veratrin" group have been misnamed. It is not found at all in species of the genus *Veratrum*. *Veratrum* contains no veratrin but, as is now well known, is a mixture of quite different alkaloids. The alkaloids of the "veratrin" group are, as is generally known, obtained from sabodilla seeds. These are the seeds of a species of *Zygadenus*. Hunt was the first to show that the *Zygadenus Venenosus* of western U. S. contains the same or similar alkaloids. Slade confirmed this, and Heyl and his collaborators obtained a crystalline alkaloid, apparently belonging to this group, from *Z. intermedius*.

In the investigation herein reported, similar alkaloids were obtained in crystallin form from *Z. Venenosus*, *Z. elegans*, and *Z. coloradensis*, all of them very toxic and with similar pharmacological actions. From a member of a closely related genus, *Amianthium muscatoxicum*, a similar active principle was obtained in an impure state. Apparently many of the species of this group of lilies contain "veratrin" alkaloids or alkaloids related to it.

<sup>1</sup> At the general meeting of the Amer. Chem. Soc., on Apr. 7, Prof. L. J. Henderson read one of the four papers constituting that program; its title was The chemical fitness of the world for life. An account of the meetings was published in *Science*, 1914, xxxix, p. 951 (June 26).

**Partition of the nitrogen of plant, yeast and meat extracts.** F. C. COOK. (*Animal Physiol. Lab., Bur. of Chem., U. S. Dep't of Agric.*) There is great variation in the precipitating power of the different reagents compared. Phosphotungstic acid precipitated the highest, tannin salt reagent the next highest, and acid-alcohol the lowest, percentage of the nitrogen of the seven plant, five meat and one yeast extracts examined. The formol titration method gave lower results for amino nitrogen than the Van Slyke method. All the methods showed a larger percentage of the nitrogen present in a more completely hydrolyzed state in the plant than in the other extracts. No creatin or creatinin, and very little purin, nitrogen was found in the plant extracts. The yeast extract was high in content of purin nitrogen but contained no creatin or creatinin. The nitrogen of the plant extracts was found in the filtrate from the acid-alcohol reagent. Twenty-five percent of the nitrogen of the other extracts was precipitated by this reagent. The plant extracts showed more ammonia by the Folin method than the other extracts.

**The physiological water requirement and the growth of plants in glyocoll solutions.** ALFRED DACHNOWSKI AND R. GORMLEY.<sup>2</sup> (*Lab. of Plant Physiol., Ohio State Univ.*) Though it is not known precisely to what extent amino acids occur in peat soils, the question of the ability of plants to utilize directly nitrogenous compounds in the soil other than nitrates and ammonia is of considerable importance. The data presented show that the absorption of glyocoll is not connected with the transpirational water loss but with the efficiency of the nutritive metabolism characteristic of the plant, and with the amount of water retained within the plant and involved in metabolism. Changes in body weight, if taken as the measure of growth, may be markedly altered by the quantity of metabolically retained water as well as by the deposition or removal of reserve materials in the tissues. The failure to promote continuous growth may be due to the inefficiency of glyocoll to supply material for tissue construction. This and the lack of available water enforce compensating processes in the plant.

The problem of the water requirement of plants and the criteria for the wilting coefficient, in particular the relation between the

<sup>2</sup> Dachnowski and Gormley: *Amer. Jour. Bot.*, 1914, i, p. 174.

water content of the plant and that of the soil at the time of wilting, need to be reinvestigated quantitatively. The retention of water, not transpiration, is the physiological function correlated with, and indispensable to, growth in general, and to survival and greater areal distribution of plants entering physically or physiologically arid habitats.

**A new apparatus for determining crude fiber in foods, feeding-stuffs, and feces.** A. D. EMMETT. (*Dep't of Animal Husbandry, Lab. of Physiol. Chem., Univ. of Ill.*) In crude fiber determinations it is often very difficult to transfer the last portion of insoluble residue from the flask to the Gooch crucible or funnel. The use of a beaker is an advantage, not only from the standpoint of accuracy but also with respect to saving of time.

The special feature of this apparatus is the arrangement which makes it possible to use a beaker. It consists of a specially constructed glass cone and rubber ring which prevents appreciable loss of water vapor during the boiling and thereby any increase in the concentration of the acid and alkali solutions. The inverted cone is attached to a Hopkins condenser with rubber tubing and the ring is snapped onto the lower edge of the cone. The condenser, cone, and ring are then lowered over a 400 cc. lipless beaker and adjusted until the connection between the rubber ring and beaker is tight. The entire apparatus is fastened in place by the clamp which holds the condenser. The glass cone is provided with a side-tube attachment which is so constructed that when air is drawn through the apparatus gently, the tendency to foam is greatly retarded.

**Enzymes of the central nervous system.** H. M. ENGLISH AND C. G. MACARTHUR. (*Biochem. Lab., Univ. of Ill.*) Enzyme extracts were made directly from fresh tissue with water, dilute acid, dilute alkali and dilute salt solutions, and glycerol. After several days' standing, with toluene or oil of mustard as a preservative, the extracts were examined. Lipase, peptase, nuclease, protease, peroxidase, arbutinase, salolase and dextrinase were detected.

Lipase acted on the following substances, in the order: Triacetin > monobutyryl > ethyl butyrate > olive oil > kephalin > lecithin. Sodium glycocholate, saponin and sodium phosphate were activators for lipase.



The various divisions of the brain contained the same kinds of enzymes, but in different amounts. The cerebrum extract was several times as active as that of the medulla. Gray matter is much more active than white matter.

**The carbon dioxid excretion as modified by body weight.** G. O. HIGLEY. (*Physiol. Lab., Univ. of Mich.*) This work was done with apparatus previously described.<sup>3</sup> There were nineteen subjects, students in the Univ. of Mich. The subjects, who had been engaged in lab. work for several hours preceding the experiments, reclined for 15 min. preceding the putting on of the mask and the beginning of the record. The average excretion of carbon dioxid per kilo of body weight was 6.3 mg. Wide departures from this value seemed to be due to (1) an excessive amount of adipose tissue in the body of the subject giving low results, and (2) colds and indigestion giving high results.

**Methods adapted for the determination of decomposition in eggs and in other protein food products.** H. W. HOUGHTON AND F. C. WEBER. (*Bur. of Chem., U. S. Dep't of Agric.*) The methods that are most applicable for the determination of decomposition are the Folin titration and nesslerization methods for free ammonia, Klein's modification of Van Slyke's method for amino nitrogen, and the Folin-Wentworth method for acidity of fat. Calculating the results on liquid eggs to a moisture-fat free basis, the following amounts of ammonia nitrogen in mg. per 100 gm. of material were obtained: By the Folin titration method—seconds, 11.4; spots, 14.1; light rots, 17.3; rots, 26.2; black rots, 169.6. By the Folin-nesslerization method—seconds, 12.4; spots, 20.0; light rots, 21.5; rots, 29.9; black rots, 148.6.

The amino nitrogen determination is of service in detecting liquid and dry blood rings, spots and light rots. Increase in the acidity of the fat indicates spots and worse grades of eggs.

The ammonia methods applied to herring give results indicating decomposition of the fish after standing 24 hours at about 70° F. Applied to clams, an appreciable increase in the ammonia is shown after keeping two days at a temperature of 60° F. to 65° F.

**Nephelometry in the study of nucleases.** P. A. KOBER AND

<sup>3</sup> Higley and Bowen: "The carbon dioxide excretion resulting from bicycling"; *Amer. Jour. of Physiol.*, 1904, xii, p. 311.

SARA S. GRAVES. (*Harriman Research Lab., Roosevelt Hosp., N. Y. City.*) The nephelometer can be used for the study of nucleases, if an acid egg-albumin solution is used as a precipitant. This reagent reveals the presence of 1 part of yeast nucleic acid in 1,000,000 parts of water, and is not affected in practical work by most biological substances.

**Specificity in the action of drugs on brain and heart fosfatids.** C. G. MACARTHUR AND G. H. CALDWELL. (*Biochem. Lab of the Univ. of Chicago and of the Univ. of Ill.*) If caffein, cocain, strychnin and other brain drugs show their specificity by some particular effect on brain kefalin and brain lecithin, these drugs ought to change the very sensitive calcium-chlorid precipitation-limit of the fosfatid solution. Many series of determinations gave no such result. Digitalis, strofanthin, etc., should affect heart lecithin and heart cuorin sol. in a similar way. No consistent results of this kind were noticed.

These results suggest that the fosfatids, in the condition isolated, are not concerned either through their solubilities, through changes in the state of aggregation, or through chemical combination in drug action. Probably these drugs effect more complex combinations or more labile groups of substances than those isolated.

**Proteins of the central nervous system.** H. H. MCGREGOR AND C. G. MACARTHUR. (*Biochem. Lab. of the Univ. of Ill.*) A study of the proteins of the central nervous system has been conducted by drying the fresh tissue with an air current and removing a large proportion of the lipoids by cold solvents. After this treatment, the solubility of the protein in aqueous solutions is found to be greatly increased; and the product precipitated by addition of excess of alcohol contains only slight amounts of lipoids. The protein obtained by this method contains phosphorus and has always given a slight though definite reaction for iron. Whether extracted by distilled water or by salt solutions, the protein is not precipitated by dilution: therefore the extract contains no true globulin. Treatment with weak acetic acid yields an acid-precipitated and an acid-soluble fraction. The evidence from fractional heat coagulation, and fractional salting-out, indicates chemical individuality for the product, instead of mixture of nucleoprotein and globulin.

**Reduction processes in plant and soil.** M. X. SULLIVAN. (*Bur. of Soils, U. S. Dep't of Agric.*) Plant roots possess the power to reduce ammonium molybdate to the blue oxide  $\text{MO}_3\text{O}_8$ , and to reduce a mixture of para-nitroso-dimethyl aniline and alpha naphthol to naphthol blue. The first reduction is favored by a slightly acid medium and occurs predominantly within the parenchyma cells just back of the root tip. It is probably due to nonenzymotic products. The second reduction is not particularly localized, and is retarded by dilute acids; favored by dilute alkalies. Certain soils likewise have the power to form naphthol blue from a mixture of paranitroso-dimethyl aniline and alpha naphthol. Soils possessing this power do not oxidize easily oxidizable substances such as aloin. Conversely, so far as investigated, soils acting on aloin do not form naphthol blue.

**The passage of nucleic acid from plant to medium.** M. X. SULLIVAN. (*Bur. of Soils, U. S. Dep't of Agric.*) In the water in which wheat had grown for sixteen days, with change of water every two days, material was found which was soluble in dilute alkali, precipitated by dilute acids and alcohol, contained phosphorus, gave the pentose reaction and, after hydrolysis with dilute acid gave reactions for a reducing sugar and purin bases, such as guanine (determined by color reaction and formation of the hydrochloride) and adenine (determined by color reaction). The material was judged to be nucleic acid.

**The composition and nutritive value of proprietary infant foods.** F. C. WEBER AND F. C. COOK. (*Animal Physiol. Lab., Bur. of Chem., U. S. Dep't of Agric.*) Chemical, bacteriological, and microchemical examinations were made of 36 proprietary infant foods. The nitrogenous constituents were separated, and analyses were made of the water extracts and of the ash. The foods, prepared according to the manufacturers' directions for a three-month formula, were analyzed. Charts based on the analyses of the foods and on the three-month formulas were prepared and the foods classified according to their composition and method of preparation for feeding.

The results of feeding the three-month mixtures to rats, mice and kittens, and the nutritive value and ratios of these mixtures, were tabulated. The chemical deficiencies and abnormal nutritive

ratios in some of the foods are confirmed by the results of the animal feeding tests. Foods prepared with milk and water give uniformly better results than those prepared with water alone.

A comparative study on puppies of the value of lactose and maltose was made.

**Factors influencing the quality of American sardines.** F. C. WEBER AND H. W. HOUGHTON. (*Bur. of Chem., U. S. Dep't of Agric.*) This paper embodies some of the results of the observations and studies conducted in the lab. established by the Bur. of Chem., of the Dep't of Agric., at Eastport, Maine, during the season of 1913. It does not refer to the packing of sardines in Cal.

The chief factors responsible for the lack of uniform quality in oil and mustard sardines packed on the eastern coast are: (1) Excessive pickling and salting, which removes a large amount of protein material (amino compounds), and lack of attention in securing a uniform degree of salting. (2) Use of fish containing undigested food, particularly "red feed," which is the principal cause of broken and damaged fish. (3) The steaming process, which removes a great deal of salt and flavor from the fish. (4) Insufficient drying of the fish before packing, causing in the finished product a milky appearance of the oil, a slight soapy taste, and a softening of the fish. (5) Variations in the composition of the fish at different times of the year and from different localities, particularly in regard to the fat content. (6) Quantity and quality of oil used. (7) Freezing and thawing of the packed goods.

Considering all the possibilities in connection with this industry, the most important of which is the packing for quality rather than quantity, as is done at present, it is believed that sardines could be produced in this country that would be as good in every respect as foreign sardines.

The following papers were also read and discussed—*W. D. Bancroft*: Coagulation of albumen by electrolytes.—*A. W. Dox*: A soluble polysaccharide in lower fungi.—*L. J. Henderson, W. W. Palmer and L. H. Newburgh*: Colloidal swelling and hydrogen ion concentration.—*L. J. Henderson and W. W. Palmer*: The functions of ammonium and phosphoric acid in the regulatory excretion of acid:—*W. J. V. Osterhout*: The chemical dynamics of living protoplasm.

—*R. S. Potter and R. S. Snyder*: The estimation of amino acids as such in the soil.

The following papers were read by title—*Oliver E. Closson*: The electrical stimulation of tissue.—*Max Kahn*: Comparison of the various methods for the quantitative determination of sugar in blood.—*Max Kahn*: Clinical studies of the Russo test.—*Max Kahn and C. J. Brim*: Urinary catalase in health and disease.—*Max Kahn and J. Subkis*: On the presence of oleic acid in gastric contents of patients suffering with gastric carcinoma.—*A. R. Rose*: The nitrogen distribution in feces.—*A. R. Rose and Katherine R. Coleman*: A standard in the determination of ammonia by nesslerizing with the Duboscq colorimeter.—*J. Rosenbloom*: The lipins of diseased human livers.—*J. Rosenbloom and V. L. Andrews*: The potassium content of cerebrospinal fluid in various diseases.

*Bureau of Chemistry,  
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Washington, D. C.*



# THE BIOCHEMICAL SOCIETY, ENGLAND

## Scientific programs

R. H. A. PLIMMER, SECRETARY

**February 11.** CHEM. DEP'T, MED. SCHOOL, GUY'S HOSP., LONDON BRIDGE, S. E. (5:30 P. M.).

*H. Rogerson:* The action of normal and basic lead acetates on sugars, with remarks on Rubner's tests for dextrose and lactose.

*E. L. Kennaway:* Demonstration of an electrically heated funnel.

*W. H. Hurtle:* The excretion of oxybutyric acid in a case of diabetes.

*A. Harden and R. V. Norris:* The reducing enzyme of yeast and zymine.

*T. M. Lowry:* Improved methods of polarimetric research.

*J. H. Ryffel:* Some opalescent pathological fluids containing cholesterol.

*J. H. Ryffel:* Acid production by intestinal organisms.

**March 12.** BOTANY BUILDING, IMPERIAL COLL. OF SCIENCE, PRINCE CONSORT ROAD, SOUTH KENSINGTON, S. W. (5:30 P. M.).

*V. H. Blackman and S. G. Paine:* The permeability of the pulvinus of *Mimosa*.

*W. Brown* (introduced by V. H. Blackman): The action of the extract of *Botrytis cinerea*.

*C. H. Warner:* Formaldehyde as an oxidation product of chlorophyll extracts.

*A. J. Ewins:* The constitution of pseudomuscarnine ("synthetic muscarnine").

*S. B. Schryver:* Note on the production of casein from caseinogen without proteolysis.

**May 9.**<sup>1</sup> CHEM DEP'T, ROYAL HOLLOWAY COLL., ENGLEFIELD GREEN, SURREY (4:30 P. M.).

<sup>1</sup> The Society did not meet in April.

*S. Walpole*: The direct observation of electro-phoretic movement of particles in fluids containing electrolytes.

*G. Barger*: Adsorption and the amorphous state.

*H. H. Dale* and *A. J. Ewins*: Some physiologically active derivatives of choline.

*H. Chick*: The influence of hydrogen-ion concentration and salt content upon the viscosity of solutions of euglobulin.

**June 11.** INST. OF PHYSIOLOGY, UNIV. COLLEGE, LONDON, W. C. (5:30 P. M.).

*A. Greeves* and *W. H. Hurtley*: A delicate test for pyruvic acid.

*J. A. Gardner* and *C. Leatham*: Respiratory quotients of trout.

*H. S. Raper*: The mechanism of oxidation of certain fatty acids with branched chains.

*C. Doree* and *M. Cunningham*: The production of  $\omega$ -hydroxy-methyl furfuraldehyde from carbohydrates and its influence on the estimation of pentosans and methyl pentosans.

*J. B. Leathes*, *N. C. Sharpe* and *K. C. Simon*: The excretion of nitrogen in fever.

*A. Harden* and *R. V. Norris*: The action of washed dried yeast on lactic acid in presence of methylene blue.

**July 11.** PHYSIOL. DEP'T, UNIV. OF OXFORD (4:00 P. M.).

*H. M. Vernon*: The activation of trypsinogen, especially in relation to temperature.

*P. Hartley*: The composition of the different proteins of ox and horse serum, determined by the method of Van Slyke.

*W. Ramsden*: The action of urea on proteins.

*R. H. A. Plimmer* and *R. F. Skelton*: Experiments on the estimation of allantoin in urine in the presence of glucose.

*University College, London*

SCIENTIFIC MEETINGS OF THE COLUMBIA UNIVERSITY BIOCHEMICAL ASSOCIATION, AT THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK<sup>1</sup>

PROCEEDINGS REPORTED BY THE SECRETARY,

ALFRED P. LOTHROP

I. SIXTEENTH MEETING

The *sixteenth scientific session* of the Columbia Univ. Biochem. Assoc. was held at the Columbia Med. Sch., at 4:15 P. M., on Feb. 6, 1914. Abstracts of the papers are presented here (pages 455-465) in two groups: (A) *Abstracts of papers on research by non-resident members*<sup>2</sup> and (B) *abstracts of papers from the Columbia Biochem. Dep't and affiliated laboratories*. The appended summary facilitates reference to the abstracts (120-126).<sup>3</sup>

A SUMMARY OF THE NAMES OF THE AUTHORS AND OF THE TITLES OF THE SUCCEEDING ABSTRACTS (120-126)

A

JACOB BRONFENBRENNER. The complement fixation test in tuberculosis with Besredka antigen. (120)

JACOB BRONFENBRENNER. The value of a new skin test for the diagnosis of tuberculosis. (121)

I. J. KLIGLER. A biochemical study of certain bacterial pigments. (123)

VICTOR E. LEVINE. The effect of selenium compounds upon catalase and other enzymes. (124)

VICTOR E. LEVINE. Reduction of selenium compounds in the living organism. (125)

B

MARK J. GOTTLIEB. Acetone as a precipitant of albumin. (122)

ARTHUR W. THOMAS. On the phosphorus content of starch. (126)

<sup>1</sup> Scientific meetings are held *regularly* on the first Fridays of Dec. Feb. and April, and on the first Monday in June. Proceedings of the thirteenth, fourteenth and fifteenth meetings were published in the last number of the *BIOCHEM. BULL.*, 1914, iii, pp. 302, 331 and 334.

<sup>2</sup> Members of the Assoc. who were not *officially* connected with the Columbia Biochem. Dep't when the researches were conducted.

<sup>3</sup> Previous abstracts were published in the *BIOCHEM. BULL.*: 1-44, 1912, ii, p. 156; 45-62, 1913, ii, p. 285; 63-72, 1913, ii, p. 452; 73-85, 1913, ii, p. 462; 86-107, 1913, ii, p. 541; 108-119, 1914, iii, p. 302. See also page 465.

A. ABSTRACTS OF PAPERS ON RESEARCH BY NON-RESIDENT MEMBERS<sup>4</sup>

120. The complement fixation test in tuberculosis with Besredka antigen. JACOB BRONFENBRENNER. (*Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*) At the suggestion of Prof. A. Besredka, and through his kindness in sending me tuberculin prepared and described by him,<sup>5</sup> I started a series of blood tests in tuberculosis. As the antigen contained egg yolk, in each case a control was made with a pure lipoid antigen (Noguchi).<sup>6</sup> In the first hundred cases we found a surprisingly large number that gave positive tuberculosis as well as positive Wassermann reactions. A special study of the possible co-existence of the two diseases was made, and a solution of the problem was attempted by the following several methods: (1) Seven patients, giving both Wassermann and tuberculosis reactions, were subjected to rigorous antisyphilitic treatment. At present five of them have lost the Wassermann reaction, the tuberculosis reaction persisting. (2) The presence of the two antibodies was proven by independent titration of each with five units of corresponding antigens. (3) It was found that the inactivation of serum containing both antibodies did not affect the two similarly. (4) Finally, one antibody was exhausted from the serum by repeated incubation with antigen and complement, but the other antibody remained.

The experiments described above included various controls which are very complicated and will be fully described elsewhere.

In the course of experiments through the kindness of Drs. W. H. Park and A. A. McNeil of New York, and Drs. Schildecker, Boyce and other members of the staff of this Hospital, 320 cases were examined to date, comprising these different conditions:—Typhoid fever, specific meningitis, tuberculosis, pernicious anemia, cancer, pneumonia, scarlet fever, lupus, diphtheria, syphilis, gonorrhea, trichinosis and various surgical conditions, with the following results:

<sup>4</sup> Members of the Association who were not *officially* connected with the Columbia Biochem. Dep't when the researches were conducted.

<sup>5</sup> Besredka: *Compt. rend. de l'acad. des sciences*, 156, p. 1633.

<sup>6</sup> Noguchi and Bronfenbrenner: *Jour. Exp. Med.*, 1911, xiii, p. 43.

	W+TB+	W+TB—	W—TB+	W—TB—	Total
Serum.....	31	22	31	213	297
Spinal fluid.....	4	6	0	13	23

The complete records of our cases will be published elsewhere. The general conclusions only are given here: The serum reaction with Besredka antigen seems specific. This reaction appears early in tuberculosis, yet disappears in the later stages of the disease. So far as the material on hand is concerned, it seems that either syphilis, as such, or anti-syphilitic treatment markedly lowers the resistance of the patients against tubercular infection. As to other diseases their co-existence with tuberculosis, as indicated by this reaction, does not seem to be frequent in any condition. In order to avoid any possible non-specific lipotropic reaction we propose to delipinize the antigen, which contains egg yolk. With regard to the cases that gave both reactions, we invariably found the two reactions to occur independently.

I take special pleasure in expressing our indebtedness to Prof. A. Besredka, whose kindness in placing the antigen in our hands made the studies possible.

121. The value of a new skin test for the diagnosis of tuberculosis. JACOB BRONFENBRENNER. (*Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*) In my work of last year<sup>7</sup> it was shown that tuberculous guinea pigs acquire the power of reducing the number of tubercle bacilli injected into the peritoneal cavity—that certain fixed cells of the peritoneal cavity were apparently responsible for this phenomenon, as the isolated peritoneal tissues of tuberculous animals, when removed from the body of the guinea pig, had the power of reducing the number of tubercle bacilli placed in contact with them. So far as our experiments showed, however, the intraperitoneal destruction of tubercle bacilli in tuberculous animals was not caused by circulating antibody.

It was considered desirable to determine the changes in the blood of such guinea pigs under the conditions of the tests, as it seemed improbable that the cells of the peritoneal cavity could have acquired immune properties without these being present in the blood.

<sup>7</sup> Manwaring and Bronfenbrenner: *Jour. Exp. Med.*, 1913, xviii, p. 601.



A series of experiments were undertaken to test complement deviation on the blood of tuberculous animals but the results obtained varied with the different strains of tubercle bacilli used as antigen. In general, however, experiments showed that the blood of guinea pigs, and especially of rabbits, often contains specific antibody against tuberculous antigen.

Having established this fact, an attempt was made to ascertain whether this antibody is a bacteriolysin. The series of experiments were performed both *in vitro* and *in vivo*.

In the course of this last series of experiments a very interesting phenomenon was noticed, namely, when normal guinea pigs were injected intraperitoneally with a mixture of the serum of a tuberculous guinea pig with peritoneal exudate resulting from the injection of a small amount (10,000) of tubercle bacilli in the peritoneal cavity of another highly immunized guinea pig, a local reaction often resulted at the site of inoculation, followed by a rise of temperature. This local reaction was especially pronounced when the peritoneal wall was punctured several times for the purpose of removing a sample of the exudate and in this way probably a part of the mixture was introduced from within the peritoneal cavity under the skin of the animal.

In analyzing this phenomenon it was found that the peritoneal exudate employed in these experiments could be conveniently replaced by crude tuberculin as prepared by the Board of Health of N. Y., but not very satisfactorily by a suspension of washed tubercle bacilli. The non-washed (possibly partly autolyzed) suspension of tubercle bacilli, especially if not freshly prepared, could also be used successfully. Since then a number of tests have been performed, in which guinea pig serum was replaced by the serum of tuberculous patients, and it was found that the reaction, although not very constant, is of prognostic value in tuberculosis.

While the work is still in progress, the experiments performed to date seem to show that the complement is an important factor in the phenomenon, inasmuch as heated sera failed to give this reaction, yet if treated with an addition of complement, and left at room temperature for a short time, they were reactivated. Whether the reaction is due to the liberation of an anaphylatoxin from the mixture of the serum containing the toxogenin and complement with the

antigen of the tuberculin, is a question to be decided by the experiments which are to follow.

At present I wish to call attention to this phenomenon as a possible method for the diagnosis of tuberculosis, at least in cases where the condition is not too far advanced and where there is some of the free antibody in the circulating blood.

Subcutaneous injection (0.05 cc.) of a mixture of fresh blood of patients suffering from tuberculosis (1 cc.) with tuberculin (crude, dil. 1 to 10; 0.1 cc.) into a normal guinea pig causes a local reaction similar in its aspect to a tuberculin reaction, which is of good prognostic value for the diagnosis of tuberculosis.

B. ABSTRACTS OF PAPERS FROM THE COLUMBIA BIOCHEMICAL DEPARTMENT AND AFFILIATED LABORATORIES

**122. Acetone as a precipitant of albumin.** MARK J. GOTTLIEB. In searching for a reagent which would precipitate egg white and yet not denature it, the following fact was established regarding the action of acetone: A conc. of acetone above 50 percent is necessary for the complete precipitation of protein from a 10 percent sol. of egg white in 5 percent sodium chlorid sol. The protein is denatured by the acetone in any conc., and the precipitate is entirely insoluble in water or salt sol.

**123. A biochemical study of certain bacterial pigments.**<sup>8</sup> I. J. KLIGLER. Excepting the fluorescent pigment produced by *B. pyocyaneus* and *B. fluorescens*, which has been thoroughly investigated by Gessard, Thume, Jordan and others, little work has been done on the nature of bacterial pigments. This is probably due largely to the prevailing idea that the production of pigments by bacteria is an easily suppressible function and of little specific importance. Schneider showed, however, that the extracted pigments of a number of organisms studied by him reacted in a very definite manner to various chemical reagents, such as solvents, acids, alkalis, etc. The Winslows called attention to the significance of the color of the pigment produced as a differential character among the cocci. They were able to show a striking correlation between the type of pigment produced, and other biochemical and morphological

<sup>8</sup> Conducted in part in the Biochem. Lab. of the Dep't of Public Health, Amer. Museum of Nat. Hist., N. Y. City.

characters. This correlation I was able to corroborate. In order to test the specificity of this property further, a detailed study of the chemical nature of these pigments was undertaken under the guidance of Prof. Gies.

Six organisms representing the different genera established by the Winslows were selected as follows:

Albococcus—white pigment

Aurococcus—orange pigment

Micrococcus—yellow pigment

Sarcina lutea—yellow pigment

Sarcina aurantiaca—orange pigment

Rhodococcus—red pigment.

These were first grown on a large number of media of different compositions, in the hope of obtaining some clue as to the chemical nature of the pigments from the nutrient substances needed for their synthesis. This hope was not realized. Peptone or some soluble protein was essential for pigment production by the cocci. In general it appeared that optimum growth conditions were also the most favorable conditions for color formation. Moderate acidity was best. Purin bases and creatin had no effect. Cholesterol had a marked influence on the yellow pigment, which showed a decided greenish tinge during the first few days of growth; it had no effect on the other organisms. Slight variations were observed with other substances but none of them seemed definite or characteristic.

An attempt to isolate the pigments from the other organic substances was not successful. The quantity obtained is so minute at best, and so easily lost in the purifying process, that a sufficient amount of the pure material could not be obtained. It was possible, however, to work out a number of the reactions of the pigments studied when they were extracted in a partially pure state, and considerable light was thrown by this procedure upon their mutual relationships.

The pigments are all soluble in alcohol, ether and chloroform. They may be precipitated from alcoholic sol. with lead acetate or water. Any such precipitate carries the pigment along with it, but the latter may be re-extracted with alcohol. In the purest state I was able to obtain, the microscopic picture was that of a colorless hyalin film with a number of colored granules distributed more or less irregularly in it.

A study of the diffusibility of these substances through rubber and collodion membranes indicates that they are not true lipochromes. They diffuse readily from alcohol to alcohol, but do not diffuse from alcohol to ether or ether to alcohol. An alcohol-water system causes a precipitation of the chromes in the bag. This precipitate may be redissolved in alcohol.

The reactions of these pigments with various reagents are suggestive. They are all decolorized by strong acids, and oxidizing and reducing agents. Their behavior to alkalis is highly specific. The yellow chrome is not altered at all by alkalis. The two orange colors react in totally different ways. The orange of the aurococcus is turned to yellow and regains its orange tinge on neutralization; that of the *S. aurantiaca* is turned to a pink. The red chrome is unaffected, and the white is not a distinct pigment. Dilute acid changes the aurantiaca chrome to yellow and leaves the other unaffected. Conc. sulphuric acid turns the evaporated residues of all the pigments to dirty bluish or greenish. This is a characteristic lipochrome reaction.

A hint as to the relationship of these organisms may be obtained from the reactions of their pigments. Yellow is the stable color recurring in all the forms and is apparently basic for the group. The chrome of *S. aurantiaca* is related both to the yellow and red, and may form a connecting link between them, while the orange of the aurococcus is related to the yellow on the one hand and grades into the white on the other. It might be surmised, from the pigment relations of the group, that the yellow micrococci are most primitive, leading up on the one hand by way of the aurococci to the albococci and streptococci, and on the other by the yellow *sarcinae* and *S. aurantiaca* to the red-pigment forms.

**124. The effect of selenium compounds upon catalase and other enzymes.** VICTOR E. LEVINE. The compounds of selenium employed were selenium dioxid (selenious acid), selenic acid, sodium selenite, sodium selenate and potassium selenocyanate. The effect upon catalase was determined as follows: Healthy normal dogs were bled to death from a femoral artery, under local cocaine anaesthesia. Weighed amounts of defibrinated blood and tissues were ground with sand in a mortar, treated with 40 c.c. of dist.



water and 10 c.c. of chloroform, and extracted for 24 hr. These served as controls. Equal amounts of blood and tissues were treated in the same manner, except that the distilled water was substituted by 0.05 percent sol. of a selenium acid or a 0.1 percent sol. of a selenium salt. A definite vol. of the filtrate was treated with 5 c.c. of Oakland dioxygen and the catalytic power of the filtrate, as measured by the vol. of oxygen evolved, determined for every 30 seconds. According to figures obtained for normal tissues the liver, blood and kidneys display the greatest catalytic activity.

These compounds of selenium exerted marked inhibitory effects on catalytic activity. Thus, 10 gm. of defibrinated blood evolved 52 c.c. of oxygen in 7 min.; another sample of the same blood, treated with 0.05 percent selenium dioxid, evolved 49.8 c.c. in 21 min.; a third sample, treated with 0.05 percent selenic acid, evolved 52.6 c.c. in 14 min. Blood from another dog yielded 44.8 c.c. in 9 min.; another sample of the same blood, treated with 0.1 percent potassium selenocyanate, evolved 37.7 c.c. in 22 min. Control liver-extract yielded 52.7 c.c. in 2 min.; selenited liver-extract yielded 50.2 c.c. in 8.5 min.; selenated liver-extract, 49.5 c.c. in 4 min. Another control liver gave 45.5 c.c. in 5.5 min., while another sample of the liver treated with potassium selenocyanate yielded 41.7 c.c. in 13.5 min.

Generally speaking, the blood, liver, kidney, lung and spleen showed marked decrease in catalytic activity, the decrease being as much as 60 percent or more. Compared on the basis of equipercantages, it was found that selenium dioxid was more harmful than selenic acid and that sodium selenite produced greater inhibition than sodium selenate. It is interesting to note, however, that colloidal selenium (prepared by the reduction of sodium selenite by glucose) induced slight acceleration in catalytic activity. Tissues of dogs killed with selenious acid, with selenic acid, or with potassium selenocyanate, showed no reduction in catalytic values. These findings indicate that these selenium compounds were decomposed in the animal organism with the formation of substances that had no inhibiting effect on catalytic action.

The influence on salivary amylase was determined by Wohlge-muth's method. Small amounts of sodium selenite (neutralized)



and sodium selenate (0.05–0.1 percent) induced slight effects on ptyalin. In the presence of 0.05 percent sodium selenite and, more markedly, in the presence of 0.05 percent sodium selenate, the activity of amylase seemed slightly increased. The results obtained for peptolysis showed that selenious or selenic acid could replace hydrochloric acid in the process. Selenious acid was slightly inhibitive, while selenic acid resembled sulfuric acid in the marked inhibition shown towards proteolysis. Sodium selenite (neutralized) and sodium selenate (0.01 to 0.02 percent) had little or no effect on peptic activity. Higher concentrations produced inhibition, this being more marked with sodium selenite than with sodium selenate. Potassium selenocyanate, even in minute amounts, inhibits peptic digestion, due, in part, probably, to mechanical interference by the brick red precipitated selenium, which completely covers the substrate (fibrin); or, possibly, to the presence of the compound that results from the acid decomposition of potassium selenocyanate. Slight amounts of sodium selenate and potassium selenocyanate had no effect on tryptic activity. Neutralized sodium selenite inhibited even in small quantities.

Sodium selenate and potassium selenocyanate (0.05–0.5 percent) had no influence on rennin. Coagulation was retarded by conc. of neutralized sodium selenite above 0.2 percent. Sodium selenite and sodium selenate had but slight effect on the souring of milk. Potassium selenocyanate showed an inhibitory effect, the amount of inhibition being directly proportional to the conc. of the salt.

Sodium selenate and potassium selenocyanate had no effect on pancreatic lipase. Sodium selenite showed slight inhibition, the effect produced being proportional to the conc. Selenium dioxid and selenic acid markedly increased hydrolysis (acid content).

Selenium dioxid in conc. of 0.5 percent had a marked inhibition on alcoholic fermentation. In a 2.5 percent sol., fermentation still occurred but was suppressed entirely in a 3 percent sol. Sodium selenite (alkalin) inhibited the evolution of carbon dioxid. Selenic acid, even in a conc. of 0.04 percent, exercised an inhibitory influence over zymase. Very little carbon dioxid was evolved in a 0.2 per cent sol., while sol. containing 0.5 percent or more gave no evidence of carbon dioxid formation. Sodium selenate accelerated

alcoholic fermentation. The effect produced by potassium selenocyanate seemed to be variable, although in general the inhibition produced by conc. lower than 2.5 percent was slight.

(The details of this research will be included in the author's Ph.D. dissertation, soon to be published. *Ed.*)

**125. Reduction of selenium compounds in the living organism.** VICTOR E. LEVINE. *Plant materials* (apple pulp and potato pulp) reduce sodium selenite to brick-red selenium; an alkalin reaction favors the process. Boiled material is practically devoid of reducing influence. Yeast reduces selenious acid, selenic acid and sodium selenite to elemental selenium, but it does not reduce sodium selenate. Reduction is observed, even when there is no production of carbon dioxide, a fact which suggests that, in addition to the alcoholase, zymase, yeast contains a specific reducing enzyme, which withstands the toxic action of the compounds of selenium better than zymase itself. The red selenium is deposited in the cell-body, the surrounding liquid remaining colorless. The cells can be decolorized by washing with potassium cyanid.

Unboiled *milk* containing a small proportion of sodium selenite (room temp.) shows reduction within 1-3 days; boiled milk shows no evidence of reduction in that time. Unboiled milk protected with toluene does not reduce as readily as milk exposed to the air.

*Animal tissues* also reduce sodium selenite. Fresh liver, spleen, heart, lung, kidney, pancreas, small intestine, large intestine and stomach, preserved with toluene and incubated at 37.5° C., reduced a 0.5 percent alkalin sol. of sodium selenite. The liver and spleen caused most reduction. Portions of striped muscle, testicle, thyroid, submaxillary gland and sublingual gland gave negative results. Tissues heated on a water-bath for about 10 min. failed to effect reduction. Fresh liver, however, heated or unheated, reduced sodium selenite. Tissues to which chloroform had been added had no reducing power. Filtered chloroform extracts also did not reduce, although liver extract did so on the first or second day, and the spleen on the third or fourth day. The other extracts failed to effect reduction even after two weeks. Toluene-preserved, unfiltered extracts, kept at room temp. for 24-36 hr., showed reduction at the end of 24 hr. only in the cases of liver, pancreas and small

intestine. Selenium dioxid and selenic acid were also reduced, but sodium selenate was not.

Selenium compounds *injected into the animal body*, undergo reduction. Some of the selenium escapes from the organism in the form of volatile organic selenid, some is precipitated extracellularly in the tissues as dark red-brown granules, the liver and spleen containing by far the largest amount of such deposited selenium. The microscopic examination of the histologically stained tissues of a dog that had received 2 mg. of selenium dioxid per kilo revealed the presence of selenium in these two organs. With sodium selenite, selenium was found more widely distributed: in the liver, spleen, kidney, lung, pancreas, heart, stomach and intestine. These tissues also showed marked reduction near hemorrhagic clots. Other tissues occasionally exhibited reduction only within such areas. A lethal dose of selenic acid was followed by deposition of the granules in the spleen and liver. The lungs, which were found to be extremely congested, also showed reduction. Selenium pigmentation with potassium selenate was slight in comparison with that produced from sodium selenite, and but few granules were found in the spleen, pancreas and liver. In the case of potassium selenocyanate, reduced selenium was found in the liver, spleen, lung, kidney, pancreas, heart, brain (only in hemorrhagic spots), muscle (only in similar spots), and stomach. The reduction of selenium compounds seems to be a detoxicating process; selenium itself displays very little toxicity.

*Living bacteria* reduce selenious acid, selenic acid and sodium selenite to elemental selenium, but do not reduce sodium selenate. Selenium may be also deposited from potassium selenocyanate, as a result of acid decomposition. The precipitated selenium follows the path of bacterial growth. For such tests, the medium used should not contain reducing chemical substances such as glucose and lactose.<sup>9</sup> Reduction is proportional to the intensity of growth. Selenious acid, selenic acid and, less markedly, sodium selenite, inhibit growth. The amount of retardation depends upon the nature of the organism. *Streptococcus pyogenes* was found to be more sensitive than *Bacillus coli*. The bacilli of symptomatic anthrax, edema, and tetanus suffer very markedly in growth, even in the

<sup>9</sup> Levine: Biochemical studies of selenium; *BIOCHEM. BULL.*, 1913, ii, p. 552.

presence of minute proportions of any of these compounds. Sodium selenate and potassium selenocyanate do not retard growth. Neither selenium dioxid nor sodium selenite can be used as a *differential test* for aerobic or anaerobic organisms, since several of the latter class effected reduction. There seems to be no specific relationship between selenium reduction and hydrogen sulfid production, as Gloger<sup>10</sup> maintained in the case of tellurium compounds, since microörganisms, such as *B. acidi lactici*, *B. diphtheriæ*, *B. pseudodiphtheriæ*, *B. tuberculosis*, that produce no hydrogen sulfid or only traces, are also capable of reducing selenium dioxid or sodium selenite.

(The details of this research will be included in the author's Ph.D. dissertation, soon to be published. *Ed.*)

**126. On the phosphorus content of starch.** A. W. THOMAS.  
(See page 403 of this issue of the BULLETIN.)

## II. SEVENTEENTH MEETING

The seventeenth scientific meeting of the Assoc. was held at the Columbia Med. Sch., at 4:15 P. M., on April 3, 1914. The appended summary facilitates reference to the abstracts (127-132) of the papers presented, pages 466-471.

### A SUMMARY OF THE NAMES OF THE AUTHORS AND OF THE TITLES OF THE SUCCEEDING ABSTRACTS (127-133)

#### A

OLAF BERGEIM, M. E. REHFUSS AND P.

B. HAWK. The stimulation of the gastric secretion in the human stomach by means of water. (127)

ALLAN EUSTIS AND L. C. SCOTT. Isolation of vitamin from rice polishings. (128)

F. H. FALLS AND WM. H. WELKER.

The appearance of non-colloidal, ninhydrin-reacting substances in the urine under normal and pathological conditions, and during pregnancy. (129)

ROSS A. GORTNER. Note on the solu-

bility of urea in ether, and of uric acid in alcohol and in ether. (130)

ROSS A. GORTNER. Studies on the chemistry of embryonic growth. II. Comparative analyses of the eggs and of the newly hatched larvae of the giant salamander, *Cryptobranchus allegheniensis*. (131)

#### B

WILLIAM J. GIES. Comment on parathyroidectomy, with an exhibition of Ivanoff's drawings on the location of the parathyroid glands in guinea pigs and field mice. (132)

<sup>10</sup> Gloger: Kalium tellurosum in der Medizin und Hygiene; *Centralbl. f. Bakteriöl.*, 1906, xl, p. 584.



## A. ABSTRACTS OF PAPERS ON RESEARCH BY NON-RESIDENT MEMBERS

127. The stimulation of the gastric secretion in the human stomach by means of water. OLAF BERGEIM, M. E. REHFUSS AND P. B. HAWK. (*Lab. of Physiol. Chem., Jefferson Med. Coll., Phila.*) A number of experiments have been made on individuals with normal and pathological stomachs. The data indicate that water produces a pronounced stimulation of the gastric secretion. In some instances 200-500 cc. of water were given on an empty stomach and portions of the fluid were withdrawn from the stomach at 5-15 minute intervals until the stomach was empty. In other instances, the water was given 2-3 hr. after an Ewald test meal, *i. e.*, when the stomach was empty. The Rehfuss tube was used in these tests. This tube is similar to the Einhorn tube with the exception of the tip which is much heavier and so slotted as to permit of more satisfactory withdrawal of samples of juice.

Determinations of total acidity, free acidity, and pepsin content were made. In general the acidity increases progressively after the introduction of water and reaches its maximum in 45 min. to 1½ hr. afterward. The most pronounced acidity thus far obtained was one of 119.5 (in terms of *n*/10 sodium hydroxid sol.) secured 50 min. after the introduction of 500 cc. of cold tap water (10.5° C.). The peptic activity also increases under the influence of the water.

A general investigation of gastrointestinal secretions obtained with this tube is under way.

128. Isolation of vitamin from rice polishings. ALLAN C. EUSTIS AND L. C. SCOTT. (*Lab. of Dietetics and Nutrition, Med. Dep't, Tulane Univ., New Orleans, La.*) Funk found that the substance which cured pigeons of the so-called *Polyneuritis gallinarum* could be precipitated by phosphotungstic acid. This precipitate, decomposed with barium hydroxid, yielded on evaporation in vacuo a residue containing the curative principle. He found, further, that the residue freed from purin bases with excess of silver nitrate and made alkaline with powdered barium hydroxid gave a precipitate. This, decomposed with hydrogen sulfid and concentrated, yielded 0.4 gm. of crystals, which proved to be very active and which he called vitamin. The method of preparation is that used for isolating mem-



bers of the pyrimidin group, and he therefore concluded that the new compound must contain a pyrimidin ring.

Funk's results were obtained with 54 kg. of rice polishings. Since it was not practicable to work up such a large quantity, 2 kg. were used in a preliminary exp. These were extracted, for 4 days, with 8 liters of 0.5 percent sol. of hydrochloric acid in alcohol. The filtered extract was conc. in vacuo at 37-50° C. The conc. syrup, diluted with water, was neutralized with barium hydroxid, eliminating the phytin at once and forming soaps with the fats. The heavy precipitate was filtered off and sulfuric acid to approximately 5 percent added to the filtrate. To this, phosphotungstic acid was added in excess, the precipitate was filtered off on a Büchner funnel, washed and decomposed with excess of barium hydroxid by grinding with water in a mortar. A distinct ammoniacal odor was noted, indicating decomposition of amino compounds. The mass was then filtered, the filtrate freed from excess of barium with carbon dioxid and evaporated to a small volume, from which the remainder of the barium was removed with dilute sulfuric acid.

The conc. filtrate, containing the merest trace of acid, cured chickens inside of 4-6 hr. when injected into the pectoral muscles. The quantity of substance was small, and the cures by no means uniformly obtained, but two experiments with chickens in violent convulsions demonstrated beyond a doubt that some curative substance must have been present.

An attempt was made, by further treatment of the extract from 12 kg. with the silver nitrate-barium hydroxid method, to obtain even a minute quantity of *pure* vitamin, but without success.

129. **The appearance of non-colloidal, ninhydrin-reacting substances in the urine under normal and pathological conditions, and during pregnancy.** F. H. FALLS AND WM. H. WELKER. (*Lab. of Med. Research and Physiol. Chem., Coll. of Med., Univ. of Ill., Chicago, Ill.*) In this investigation 124 urines from normal, pathological, and pregnant cases, were studied with respect to their reaction with ninhydrin. For the removal of colloidal substances an excess of aluminium hydroxid cream was used and the ninhydrin test was applied to the filtrate. A series of urines were also studied in which the ninhydrin test was applied directly to

the urines, to the filtrates from aluminium hydroxid mixtures, and to the diffusates through parchment and collodion bags. It was found that removal of the colloidal substances from the urine favored the production of the blue color typical of the reaction produced by amino acids with ninhydrin. A positive ninhydrin reaction on urine from which the colloidal substances have been removed is of no value for the diagnosis of pregnancy, for such positive reactions are obtained in normal, and a large series of pathological cases, as well as in cases of pregnancy. Furthermore, in some cases of pregnancy the reaction is either very faint or absent altogether.

**130. Note on the solubility of urea in ether, and of uric acid in alcohol and in ether.** ROSS A. GORTNER. (*Biochem. Lab. of the Station for Exp. Evolution, Carnegie Inst. of Washington.*) In stating the solubilities of urea in ether and of uric acid in alcohol and in ether, Beilstein, and all other authorities I have examined, unite in the statement that no solution occurs. Thierfelder<sup>11</sup> states that urea is "unlöslich" in ether and uric acid is "gar nicht löslich in alkohol oder aether" (p. 170). These statements are true regarding *any appreciable solubility* in 100 cc. of the solvent, but when the solubility is tested in a Soxhlet apparatus the weight of the substance dissolved is appreciably large.

The ether used in the following experiments was Kahlbaum's "ueber Natrium destilliert," the alcohol was Squibb's "absolute," the urea and uric acid were of Kahlbaum's best grades. Both the alcohol and the ether were from freshly opened containers and during the extractions the contents of the apparatus were protected from atmospheric moisture.

*Solubility of urea in ether.* 0.3255 gm. of urea was extracted in a Soxhlet app. with anhydrous ether for 48 hr. Within a few hours after the extraction was started, needle shaped crystals began to separate in the flask and at the end of the extraction it was found that 0.0720 gm. of urea had been dissolved. A rough estimation, based on the vol. of the liquid syphoning and on the number of syphonings in an hour, gives the solubility of urea as 0.0004 gm. in 100 cc. of ether.

*Solubility of uric acid in ether.* Approximately 0.75 gm. of uric

<sup>11</sup> Thierfelder: Hoppe-Seyler's *Handb. d. physiol. u. pathol. chem. Anal.*, 1909, p. 145 (Berlin).

acid was extracted in a Soxhlet app. for 48 hr. with anhydrous ether. Only 0.0010 gm. dissolved. The ether was evaporated and the dry residue tested for uric acid by the murexid test with negative results. Uric acid is, therefore, *insoluble* in ether.

*Solubility of uric acid in alcohol.* Approximately 0.81 gm. of uric acid was extracted with absolute alcohol for 48 hr. The alcohol in the flask became milky due to the separation of uric acid crystals and at the end of the extraction 0.0260 gm. had dissolved. Thinking that perhaps there might be some impurity in the uric acid which was soluble in alcohol, the residue from the first extraction was again extracted for 36 hours with fresh alcohol and a further loss of 0.0197 gm. occurred. A rough estimation, based on the vol. and number of syphonings, gives the solubility of uric acid in alcohol as 0.00008 gm. in 100 cc.

*Conclusions.* Inasmuch as nearly all tissue analyses are carried out by extraction methods a very appreciable amount of urea may be dissolved by ether, although the solubility of urea in ether is probably not much greater than 0.0004 gm. in 100 cc.

Uric acid is insoluble in ether but is very slightly soluble in absolute alcohol (approximately 0.00008 gm. in 100 cc.) *This solubility, however, is sufficient to dissolve 0.0260 gm. in a 48 hr. extraction.*

Inasmuch as these experiments were made with a Soxhlet app. it seems probable that greater amounts would be dissolved in extractors operating at the temp. of the boiling solvent.

*"Insoluble"* in a biochemical sense should mean *no appreciable solubility after a 48 hr. extraction in an extraction apparatus.*

131. Studies on the chemistry of embryonic growth. II. Comparative analyses of the eggs and of the newly hatched larvae of the giant salamander, *Cryptobranchus alleganiensis*.<sup>12</sup> ROSS A. GORTNER. (*Biochem. Lab. of the Station for Exp. Evolution, Carnegie Inst. of Washington.*) Analyses of the eggs and larvae of *Cryptobranchus* included ether-soluble, ether-insoluble but alcohol-soluble, and ether- and alcohol-insoluble (protein) fractions. The nitrogen partition was determined on the first two fractions after boiling for 18 hr. with hydrochloric acid (1.115 sp.g.) and the

<sup>12</sup> For an abstract of the first paper in this series see Proc. Columbia Univ. Biochem. Assoc., BIOCHEM. BULL., 1913, ii, p. 463.

protein fractions were analysed by Van Slyke's method. The following conclusions are drawn:

There are two yellow pigments in the eggs, one being soluble in ether, the other insoluble in ether but soluble in alcohol.

There is a total loss in dry weight (carbon dioxide and water) during the development of 100 eggs to the hatching stage of 0.0969 gm.

There is a *gain* of fats in the development of the egg to larva, the ether extract rising from 1.1182 gm. per 100 eggs to 1.2747 gm. per 100 larvae.

There is a *loss* in ether-insoluble but alcohol-soluble substance of from 0.6630 gm. in 100 eggs to 0.6179 gm. in 100 larvae.

There is a loss in the protein fraction, the weight falling from 4.0256 gm. in 100 eggs to 3.8278 gm. in 100 larvae.

There is neither gain nor loss of nitrogen in development; 100 eggs = 0.5849 gm. N., 100 larvae = 0.5845 gm. N.

There is a gain of nitrogen in the ether-soluble portion of from 0.0025 gm. to 0.0045 gm. This indicates a synthesis of 0.1174 gm. of lecithin (1.73 percent N.) providing all of the nitrogen in the ether-soluble portion is counted as lecithin.

There is a gain of nitrogen in the ether-insoluble but alcohol-soluble portion of from 0.0070 gm. to 0.0111 gm. The nitrogen in this fraction is largely basic nitrogen, probably purin or pyrimidin bases.

There is a loss of 0.0066 gm. of nitrogen from the protein fraction. Nearly all of this loss comes from the mon-amino acids.

Tangl and Farkas<sup>13</sup> hypothesis, as postulated for the trout eggs, does not hold true, *i. e.*, that when there is a gain of fats this gain comes from the glycoproteins, the nitrogen of the protein being retained in the organism in the form of urea or uric acid. It seems probable that the carbohydrate portion of a glycoprotein (ovomucoid?) furnishes the "Entwicklungsarbeit" of *Cryptobranchus* eggs, and that the energy released by the breaking down of the carbohydrate is more than sufficient for the energy of development and as a result fat is synthesized. The nitrogen of the glycoprotein however is not broken down to either urea or uric acid. Urea nitrogen would appear in the ether-soluble portion (see preceding abstract) but an increase of only 0.00035 gm. of ammonia nitrogen

<sup>13</sup> Tangl and Farkas: *Arch. ges. Physiol.*, 1908, civ, pp. 624-38.



was observed in this fraction. If uric acid were formed a considerable part, if not all, would be dissolved by the alcohol (see preceding abstract), but there is only a comparatively slight increase of nitrogen in this fraction.

I therefore conclude that the greater part of the "Entwicklungsarbeit" of *Cryptobranchus* comes from a carbohydrate and, if this carbohydrate is in the form of a glycoprotein,<sup>14</sup> the amino acids are not broken down to urea or uric acid but are utilized in part in their original form and in part to furnish the nitrogen for lecithin and other nitrogenous compounds necessary for the development of the growing embryo.

B. ABSTRACT OF A PAPER FROM THE COLUMBIA BIOCHEM. DEP'T

**132. Comment on parathyroidectomy, with an exhibition of Ivanoff's drawings on the location of the parathyroid glands in guinea pigs and field mice.** WILLIAM J. GIES. The author referred to various operative procedures for the removal of the parathyroid glands from small animals, especially Erdheim's method, and called particular attention to Ivanoff's illustrated dissertation—one of the few available sources of information regarding the relative positions of the thyroids and parathyroids in small rodents.<sup>15</sup> A copy of this dissertation, from the Surgeon General's Library (Washington, D. C.), was shown and discussed.

*(The proceedings of the June meeting will be published in the next number of the BULLETIN)*

*Biochemical Laboratory of Columbia University,  
College of Physicians and Surgeons,  
New York*

<sup>14</sup> More material will be secured another year to determine this point.

<sup>15</sup> Ivanoff: Contribution a l'etude des glandules parathyroïdes chez les rongeurs (cobaye et mulot). Thèse: Geneva, 1905.



## DOCTORATES IN BIOLOGICAL CHEMISTRY

Conferred by American Universities, 1913-'14

The names of recent recipients of the Ph.D. degree in biochemical science, with the subjects of the dissertations, are arranged below in university groups:

**Brown University.**—*George Henry Robinson*: Isolation, identification and serum reactions of typhoid and paratyphoid bacilli.

**Clark University.**—*Lillian Rosanoff*: Theory of the catalysis of sugar inversion by acids.

**Columbia University.**—*John Seaman Bates*: Chemical utilization of southern-pine waste.—*Sidney Born*: The chemical constitution of invertase.—*Louis Otto Kunkel*: Physical and chemical factors influencing toxicity of inorganic salts to *Monilia sitophila* Mont. Sacc.—*Marguerite Thuron Lee*: A study of modifications of the biuret test.—*Victor Emanuel Levine*: Biochemical studies of selenium.—*Charles Packard*: The effect of radium on the development of *Nereis*.—*Ernest Lyman Scott*: The content of sugar in blood under common laboratory conditions.

**Cornell University.**—*Jean Broadhurst*: A study of the habitats and the morphological and physiological characters of streptococci.—*Jehiel Davidson*: A comparative study of the effect of coumarin and vanillin on wheat grown in soil, sand and water cultures.—*Frank Elmore Rice*: Studies on the action of erepsin.—*Clarence McKinlay Sherwood*: A study of Stokes' neutral red reaction as applied to the sanitary examination of water.

**Harvard University.**—*William T. Bovie*: The action of ultraviolet light on protoplasm.—*Francis Bullard Kingsbury*: I. A contribution to the rôle of bile in fat absorption. II. The determination of benzoic acid in the urines of the rabbit and the dog.—*James Lucien Morris*: Protein metabolism of the rat, with special reference to tumor problems.—*James Batcheller Sumner*: The formation of urea in the animal body.

**Indiana University.**—*Clarence Edmunds Edmondson*: The effects of thyroid and thymus extract upon the growth and reproduction in *Paramecium caudatum*.

**Johns Hopkins University.**—*Elmer J. Lund*: The relations of *Bursaria* to food: I. Selection in feeding and in extrusion.—*Annabella Elliott Richards*: The partial enzymotic hydrolysis of yeast nucleic acid.

**New York University.**—*John Daly McCarthy*: The influence of certain drugs on the efficiency of mental work.

**University of California.**—*Roy Elwood Clausen*: On the behavior of emulsin in the presence of collodion.—*Rosalind Wulzen*: The pituitary gland in its relationship to the early period of growth in birds.

**University of Chicago.**—*John William Edward Glattfeld*: The oxidation of *d*-glucose in alkaline solution by air as well as by hydrogen peroxid.—*Edward Maris Harvey*: Some effects of ethylene on the metabolism of plants.—*Ole Olufson Stoland*: The influence of parathyroid tetany on the liver and the pancreas.

**University of Illinois.**—*William Ernest Carroll*: Effect of the amount of protein consumed upon digestion and protein metabolism in lambs, and upon the composition of their flesh and blood.—*Harold Hossack McGregor*: The proteins of the central nervous system.—*John Hamilton Whitten*: The effect of kerosene and other petroleum oils on the viability and growth of *Zea mays*.

**University of Michigan.**—*Anton Augustus Schlichte*: The changes which take place in hides during the unhairing process.

**University of Minnesota.**—*Harold Hiram Brown*: Contribution to our knowledge of the chemistry of wood; Douglas fir and its resin.

**University of Pennsylvania.**—*Charles Blizard Bazzoni*: The destruction of bacteria through the action of light.

**University of Wisconsin.**—*Elbert T. Bartholomew*: Physiological changes causing black heart in potatoes.—*Ralph Howard Carr*: A study of the non-protein form of nitrogen in alfalfa.—*Harry Alfred Curtis*: A quantitative study of some photochemical reactions.—*Howard Austin Edson*: Damping off and root decay of sugar beets.

**Yale University.**—*Norman Robert Blatherwick*: The specific rôle of foods in relation to the composition of the urine.—*Lewis Hill Chernoff*: Pyrimidin nucleosids.—*Samuel Goldschmidt*: The

metabolism of an isomer of xanthin and some isomers of the methylxanthins.—*Albert Garland Hogan*: Studies on the parenteral utilization and the metabolism of sugars.—*Joel Andrew Sperry*: A biochemical study of the behavior of bacteria towards pure unchanged animal and vegetable proteins.—*David Wright Wilson*: The chemistry of the nitrogenous extractives of muscle tissue.

Universities which conferred Ph.D. degrees in the natural and exact sciences, but at which there were no biochemical candidates, are named below:

Bryn Mawr College	University of Iowa
George Washington University	University of Missouri
Massachusetts Ins. of Technology	University of Nebraska
Princeton University	University of North Carolina
Stanford University	University of Virginia
University of Cincinnati	Washington University.

*Number of Ph.D. degrees awarded by American universities to biochemical candidates, 1912, 1913 and 1914*

	1912	1913	1914	Total	1912	Women 1913	1914
Brown University .....	1	0	1	2	0	0	0
Clark University .....	0	0	1	1	0	0	1
Columbia University .....	11	7	7	25	1	0	1
Cornell University .....	5	2	4	11	0	1	1
Harvard University .....	1	1	4	6	0	0	0
Indiana University .....	0	0	1	1	0	0	0
Johns Hopkins University ...	1	1	2	4	0	0	1
New York University .....	0	0	1	1	0	0	0
University of California .....	5	0	2	7	1	0	1
University of Chicago .....	8	4	3	15	1	0	0
University of Illinois .....	5	0	3	8	0	0	0
University of Michigan .....	2	0	1	3	0	0	0
University of Minnesota .....	0	0	1	1	0	0	0
University of Missouri .....	0	1	0	1	0	0	0
University of Pennsylvania ...	0	0	1	1	0	0	0
University of Wisconsin .....	4	3	4	11	0	1	0
Washington University .....	0	2	0	2	0	0	0
Yale University .....	6	4	6	16	1	1	0
Total number of awards	—	—	—	—	—	—	—
of degrees .....	49	25	42	116	4	3	5
Number of Universities							
awarding the degree .....	11	9	16	—	4	3	5

P. H. D.

# BIOCHEMICAL BIBLIOGRAPHY AND INDEX

First and second quarters, 1914 (January-June)

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**Explanation of abbreviations, arrangement, notation, etc.** **BIBLIOGRAPHY.** *Titles of papers* are freely shortened, minor words ignored, common terms conveniently abbreviated or chemical symbols substituted; *surnames* of collaborators are connected by hyphens; most *punctuation marks* are omitted—all for the sake of condensation. Heavy faced Roman numerals indicate *volumes*; heavy faced Arabic numerals designate *numbers and dates of issue* (slanting lines separate numerals for months and days). *Bibliographic items* begin with em dashes. When two or more papers by the same author occur together, they are duly numbered, and separated by semicolons, but follow the same em dash. Numerals preceding italicized names of authors indicate *sequence in the bibliography (index numerals)*; numerals preceded by commas, at the ends of items, indicate *initial pages of the corresponding papers*.

**INDEX (SUBJECTS).** The numerals in the indices (pp. 480, 487) correspond with the numbered items in the bibliography. *Pages are not indicated.* Numerals held in groups by hyphens are plain abbreviations in accord with the indications of the first numeral of each such series (see footnote, p. 480). Abbreviations of words in the index are similar to those in the bibliography. Each *group of index references* is terminated by a semicolon; commas mark off *subdivisions of a general index subject*. *Names of authors are not indexed.*

**JOURNALS INCLUDED:** *Biochemische Zeitschrift (B.Z.)*, *Zeitschrift für physiologische Chemie (Z.p.C.)*, *Journal of Biological Chemistry (J.B.C.)*, *Biochemical Journal (B.J.)*, *Biochemical Bulletin (B.B.)*.

**PRACTICAL USE OF THE BIBLIOGRAPHY.** The bibliography is helpful from several standpoints. Thus, if it is desired to ascertain whether the journals included in the bibliography contain any papers (during the given quarter) on a particular subject, *e. g.*, lipins, find the key word in its alphabetical place in the index and turn to the items in the bibliographic sequence indicated by the index numerals [in this case in the first index, page 480, 20, 64, (*lipoprotein*) 25, 26, 27]. The abbreviated items thus identified give the names of authors and suggest the nature of the corresponding papers (ten papers in the case selected for illustration), and help the reader to decide whether to examine the original publications. When the index gives a negative answer to an inquiry, a large mass of literature is removed from further consideration. During the intervals between publication of the indexes of journals, *Zentralblätter* and year books, this running bibliography directs the reader to most of the main tracks through current literature on the leading biochemical subjects.



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<sup>1</sup> In the January number (p. 318) the preceding volume was mistakenly printed LXI instead of XVI. By an oversight the January number of the J. B. C. was included in the bibliography for the last quarter of 1913 (p. 319).

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## BIOCHEMICAL NEWS, NOTES AND COMMENT

### EDITORIAL SUB-COMMITTEE:

Alfred P. Lothrop,

William J. Gies, Joseph S. Hepburn, Benjamin Horowitz, Paul E. Howe.

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### I. GENERAL.

**Necrology.**—*Robert K. Duncan*, direc. of the Mellon Inst. for Indust. Research, Univ. of Pittsburgh.—*Herman Frasch*, for twenty years chief chemist of the Standard Oil Co.—*Joseph R. Green*, well known for his important researches in plant physiol., fellow and lecturer, Downing Coll., Cambridge; formerly prof. to the Pharmaceut. Soc. of Gr. Britain.—*S. M. Jørgensen*, pres. of the board of directors of the Carlsberg Lab., Copenhagen; successor of Prof. Barfoed, Univ. of Copenhagen.—*Fritz Jummersbach*, prof. of agricult., Munich.—*Hugo Kronecker*, prof. of physiol., Univ. of Bern.—*Adolph Lieben*, emer. prof. of general and pharmaceut. chem., Univ. of Vienna.—*Jesse J. Myers*, assis. prof. of physiol. and zool., Mich. Agric. Coll.; at the time of his death also a grad. student in physiol. chem., Yale Univ.—*Karl A. Neufeld*, assis. direc. of the food lab., Univ. of Würzburg.—*Francis H. Storer*, from 1865 to 1870 prof. of chem., Mass. Inst. of Tech., and, from 1870 to his retirement as emer. prof. in 1907, prof. of agric. chem., Harvard Univ.—*L. v. Udránsky*, prof. of physiol. chem., Budapest.—*Philippe Van Tieghem*, one of the first of Pasteur's collaborators.

**In memoriam.** LISTER. An oration on Lord Lister was delivered by Sir H. C. Cameron, at the Univ. of Glasgow, on commemoration day, June 23.—The committ. of the Lister Memor.

Fund has commissioned Sir Thomas Brock to execute a medallion portrait of the late Lord Lister, to be placed in Westminster Abbey.

Mosso. The med. faculty of Turin has decided to erect a memorial to Angelo Mosso, in the Inst. in which he taught for many years. The memorial will be unveiled on Nov. 14, 1914, the fourth anniversary of Mosso's death. Contributions should be sent to Prof. Alberto Aggazotti, Corso Raffaello, Torino.

**Honorary degrees.** Dr. *W. P. Bradley* (recently prof. of chem.), Sc.D., Wesleyan Univ.—Dr. *W. L. Dudley* (dean of the med. dep't and direc. of the chem. lab. of Vanderbilt Univ., Nashville, Tenn.), LL.D., Univ. of Cincinnati.—Dr. *J. L. Lemberger* (former pres. of the Amer. Pharmaceut. Assoc.): Phar. D., Medico-Chi. Coll., Phila.—Prof. *Jos. McFarland* (Medico-Chi. Coll., Phila.): Sc.D., Ursinus Coll.—*Provost E. F. Smith* (Univ. of Penn.), Sc.D., Yale Univ.; LL.D., Wittenberg Coll.—Sir *Edward Schäfer*, M.D., Groningen Univ., on the occasion of the tercentenary; Sc.D., Univ. of Cambridge, on the occasion of the opening of the new physiol. lab.—Dr. *Frank T. Shutt* (Dominion chem., and assis. direc. of exper. farms), Sc.D., Univ. of Toronto.—Prof. *E. H. Starling*, Sc.D., Univ. of Cambridge, on the occasion of the opening of the new physiol. lab.

**Resignations and appointments.** RESIGNATIONS. Dr. *W. P. Bradley*, prof. of chem., Wesleyan Univ.: to take charge of investigations for the U. S. Rubber Co.—Dr. *P. A. Kober*: research chem., Harriman Research Lab., Roosevelt Hosp., to take effect Oct. 1.

APPOINTMENTS.<sup>1</sup> *Beloit, Colorado*, Grinnell and Knox Coll.: Dr. *L. J. Henderson* has been appointed the prof. from Harvard Univ., for the second half of 1914-15, under the "interchange agreement" between Harvard Univ. and these four western Coll.

*Canadian Gov.*: Dr. *F. J. Birchard* (U. S. Dep't of Agric., Bur. of Chem.), chem. to the Dep't of Trade and Commerce, *Domin. Grain Research Lab.* (Winnipeg.)

*Carnegie Inst., Nutr. Lab. (Boston)*: Prof. *Raymond Dodge*, research in the psychology of nutr.; Dr. *Hans Murschhauser* (*Akadem. Kinder-Klinik, Düsseldorf*), research associate.

<sup>1</sup> In this summary institutions from which appointments were made are named in parenthesis. See, also, pages 513 and 517.



College of Hawaii (Honolulu): Prof. *A. L. Dean* (Yale Univ.), pres.

Columbia Univ.: Dr. *J. M. Nelson*, assis. prof. of organ. chem. (promotion); Dr. *W. T. Longcope*, Bard prof. of the practise of med.; Prof. Longcope was also elected med. director of the Presbyterian Hosp.

Cornell Univ.: Dr. *B. T. Galloway* (assis. sec'y of agric., previously chief of the Bur. of Plant Ind. of the Dep't of Agric.), direc., N. Y. Coll. of Agric., vice Prof. L. H. Bailey resigned, and in succession to Prof. W. A. Stocking, acting direc.

Hahnemann Med. Coll. (Phila.): Dr. *W. A. Pearson* (prof. of chem., physiol. chem., and toxicol.), dean.

Harvard Univ., Med. Sch.: Dr. *Walter R. Bloor* (Washington Univ., St. Louis), assis. prof. of biolog. chem.

Johns Hopkins Univ.: Dr. *Theodore C. Janeway* (Columbia Univ.), prof. of med.; *L. G. Rowntree*, assoc. prof. of med. (promotion); *Hans Lieb*, lect. in pharmacol.; *Eli K. Marshall, Jr.*, assoc. in pharmacol. (promotion); *Benj. B. Turner*, assoc. in pharmacol. (promotion).

Kansas Agric. Exp. Station (Manhattan): Dr. *A. C. Hogan*, assis. in animal nutr.

Mar. Biol. Lab. (Woods Hole, Mass.): Research and instr. in physiol.—Profs. *A. P. Mathews*, *R. S. Lillie*, *H. C. Bradley*, *W. E. Garrey*, *F. P. Knowlton* and Dr. *E. B. Meigs*.

Mass. Inst. of Tech.: Dr. *S. G. Prescott*, prof. of indust. biol. (promotion); *A. G. Woodman*, assoc. prof. of food anal. (promotion); *John F. Norton*, assis. prof. of chem. of san. (promotion).

Medico-Chi. Coll. (Phila.): Dr. *C. E. Vanderkleed*, prof. of analyt. chem., vice Dr. C. H. Kimberly, resigned; Dr. *A. W. Downs*, prof. of exp. physiol.

Montefiore Home (N. Y. City): Dr. *N. R. Blatherwick*, chem.

N. Y. City, Board of Est. and Apportionment: Dr. *G. C. Whipple* (prof. of san. engineer., Harvard Univ.), member of the committ. on building districts and restrictions.

N. Y. State Board of Health: Dr. *A. B. Wadsworth*, chief, lab. divis. (Albany): Prof. *C.-E. A. Winslow* (Coll. of the City of N. Y.), direc., divis. of publicity and education (New York City).



N. Y. Univ. and Bellevue Hosp. Med. Coll.: Prof. *Wm. H. Park* (prof. of bacteriol. and hygiene), dean.

Phila. Polyclin. and Coll. for Graduates in Med.: Dr. *G. W. Raiziss*, assoc. prof. of physiol. chem.

Robert B. Brigham Hosp. (Boston): Dr. *F. H. McCrudden* (Rockefeller Inst.), direc. of the laboratories.

Rockefeller Inst. for Med. Research: Dr. *Hideyo Noguchi*, member of the Inst. (promotion); Drs. *H. L. Amoss* (pathol. and bacteriol.), *T. S. Githens* (physiol. and pharmacol.), and *I. S. Kleiner* (physiol. and pharmacol.), associates (promotions); Dr. *F. L. Gates*, assis. in physiol. and pharmacol. (promotion); Mr. *C. H. Allen*, fellow in chem.; Dr. *B. S. Kline*, fellow in physiol. and pharmacol.; Mr. *J. K. Senior*, fellow in chem.

Sheffield Univ.: Mr. *A. E. Barnes*, lect. in materia med., pharmacol. and therapeutics.

Turck Research Lab. (N. Y. City): Dr. *W. von Riedl* (Cincinnati, O.), head of the dep't of bacteriol.

Univ. of Berlin: Dr. *Max Rubner*, direc., Kaiser Wilhelm Lab. for Physiol. (to be erected; see page 506).

Univ. of Bonn: Prof. *R. O. Neumann* (Giessen), prof. of hygiene.

Univ. of Minn.: Dr. *J. F. McClendon* (Cornell Univ. Med. Coll.), assis. prof. of physiol.

Univ. of Kiel: Prof. *Albrecht Bethe*, direc. of the Physiol. Inst.

Univ. of Liverpool: Prof. *J. S. Macdonald* (prof. of physiol., Univ. of Sheffield), Holt prof. of physiology.

Univ. of Penn., Med. Sch.: Dr. *A. I. Ringer*, assis. prof. of physiol. chem. (promotion); Dental Sch.

Univ. of Pittsburgh: Dr. *R. F. Bacon*, direc. of the Mellon Inst. for Indust. Research (promotion), vice R. K. Duncan, deceased.

U. S. Dep't of Agric., Bur. of Chem.: Dr. *T. C. Merrill* (recently assis. pathol., office of forest pathol. of the Bur. of Plant Ind.), med. assis.; Prof. *Löhnis* (Univ. of Leipzig), pharmacognosist.

U. S. Public Health Service—Hygienic Lab.: Dr. *M. P. Ravenel* (recently resigned the chair of bacteriol., Univ. of Wis., to accept a similar chair, Univ. of Mo.), member of the Advis. Board.—Pellagra Hosp. (Spartanburg, S. C.): Dr. *Andrew Hunter* (Cornell Univ.), biochem. investigation into pellagra.

Vanderbilt Univ. (Nashville, Tenn.): Dr. *J. W. Jobling* (Columbia Univ.), prof. of pathol.

West. Reserve Univ. (Cleveland, O.): Dr. *W. C. Alpers* (trustee, N. Y. Coll. of Pharm.), dean of the Sch. of Pharm. and prof. of pharm.

West. Univ. (London, Can.): Dr. *F. R. Miller* (dep't of physiol., McGill Univ.), prof. of physiol.

**Prizes and medals.** WINNERS OF PRIZES. *Cameron prize*, Univ. of Edinburgh: Prof. *Paul Ehrlich*, direc., path. inst., Frankfurt, in recognition of his discovery of salvarsan and other contributions to med. science.—*Emil Chr. Hansen prize*: Prof. *Jules Bordet*, direc., Inst. Pasteur, Brabant.—*Lucien Howe prize*, Med. Soc., State of N. Y.: Dr. *M. J. Schoenberg*, for his research on ocular anaphylaxis.—*Howard T. Ricketts prize*: Dr. *J. H. Lewis*, Univ. of Chicago.—*Gordon Wigan Fund*, Univ. of Cambridge (50£): Mr. *H. V. Thompson*, for investigations in organic chem., including research on the molec. weights of cellulose.

THE PARIS ACAD. OF SCIENCES offers, for 1915, the *Pourat prize* of 1000 francs for a memoir on the relations between the combined sugar of the blood and the protein constituents.

AWARDS OF MEDALS.—*Chandler gold medal* (first award): Dr. *L. H. Baekeland*, N. Y. City.—*Fothergill gold medal*, Med. Soc. of London: Dr. *John G. Adami*, McGill Univ., for his work on pathol. and its application to practical med. and surg.—*Medal of the Nat'l Assoc. of Cotton Manufact.*: Mr. *A. T. Bradlee*, for investigations on the effects of moisture in testing cotton yarns and fabrics.—*Medal of the N. Y. Sect., Amer. Chem. Soc.*: Prof. *Moses Gomborg*, Univ. of Mich., for his work on the trivalence of carbon.—*Willard Gibbs medal*, Chicago Sect., Amer. Chem. Soc.: Dr. *Ira Remsen*, Johns Hopkins Univ.

MEDALS OF THE FRANKLIN INST., STATE OF PENN.: *Elliott Cresson Gold Medals*, the highest award in its gift: Prof. *Carl P. G. Linde*, Munich, in recognition of his investigations of processes for the refrigeration and liquefaction of gases, and of his investigations of machinery for applying these processes in the manufacture of ice and for the purposes of cold storage.—Prof. *E. F. Smith*, in recognition of his leading work in the field of electro-chemistry, of his

many contributions to the literature of chem. science, and of his great service in univ. education.—Dr. *Wolfgang Gaede*, for his molecular air pump, in consideration of the very great value of this invention for the quick production of vacua beyond those hitherto obtainable.

A gold medal, known as the *Franklin Medal*, will be conferred by the Franklin Inst. for general scientific achievement. The endowment fund for the medal has been provided by the generosity of Mr. Samuel Insull, of Chicago.

**MEDAL IN AGRICULTURE.** The Royal Agric. Soc. of England offers a medal for a monograph or essay, which has not been previously published, giving evidence of *original research in any agric. subject*, or any of the cognate agric. sciences applicable to British farming.

**Associations and societies.** **AMER. ASSOC. FOR THE ADV. OF SCIENCE.** The *Commit. of One Hundred on Scientific Research*, whose appointment was authorized at the last annual meeting of the Assoc., held its first session in Washington, Apr. 20. There was a long and important discussion on scientific research in America and the means by which it can be advanced by the commit. Among the questions fully discussed were (1) the use of research funds and the establishment of a central bureau under the auspices of the Assoc., the Nat'l Acad., or the Smithsonian Inst.; (2) research work in educational institutions, the extent to which it is supported and should be regarded as the function of the institution, and its professors and instructors; (3) the research work of indust. laboratories and its relation to the universities; (4) the selection of men in universities competent to undertake research work and the preparation that should be given to them, and (5) the fuller recognition and better opportunities that should be given to those who have unusual qualifications for scientific research. It was agreed that the principal work of the commit. should be entrusted to subcommit. The whole commit. will meet at Phila., Dec. 28, 1914, at the hotel headquarters of the Amer. Assoc. Among the members of the commit. are C. L. Alsberg, R. H. Chittenden, William H. Howell, Reid Hunt, Jacques Loeb, R. M. Pearce, Ira Remsen, W. T. Sedgwick, Theobald Smith.

SOC. F. EXP. BIOL. MED. The Soc. for Exper. Biol. and Med. held a special meeting, on Saturday morning, June 6, in the lab. of the Station for Exp. Evolution, Cold Spring Harbor, L. I. After the meeting, the many members in attendance were the guests of Pres. Graham Lusk, at luncheon, in his nearby summer home.

AMER. PHILOSOPH. SOC. During the general meeting of the Amer. Philosoph. Soc., at Phila., the following papers of interest to biochemists were presented:

*April 23.*—Factors of influence in the origin and circulation of the cerebrospinal fluid: *C. H. Frazier*, prof. of clin. surg., Univ. of Penn.; Aspects and methods for the study of the mechanism of the heart beats: *A. E. Cohn*, assoc. in med., Rockefeller Inst.; The kinetic system: *G. W. Crile*, prof. of clin. surg., West. Reserve Univ.

*April 25: Symposium on the physics and chem. of protoplasm.*—The germ plasm as a stereochemic system: *E. T. Reichert*, prof. of physiol., Univ. of Penn.; Arrangement and distribution of substances in the cell: *E. G. Conklin*, prof. of zool., Princeton Univ.; Vital staining of protoplasm: *H. McL. Evans*, assoc. prof. of anatomy, Johns Hopkins Univ.; The physical state of protoplasm: *G. L. Kite*, Phipps Inst., Phila.; The physico-chemical organization of the cell: *L. J. Henderson*, assis. prof. of biol. chem., Harvard Univ.

OFFICERS-ELECT. *Amer. Med. Assoc.* Pres., *W. L. Rodman*, Phila.; 1st vice-pres., *D. S. Fairchild*, Iowa; 2d vice-pres., *W. R. Townsend*, N. Y. City; 3d vice-pres., *Alice Hamilton*, Chicago; 4th vice-pres., *W. E. Darnall*, Atlantic City; sec'y, *A. R. Craig*, Chicago (reelected); treas., *W. A. Pusey*, Chicago.

*Miscellaneous.* Royal Soc. of London: *Sir William Crookes*, pres.—Kentucky Acad. of Science: *Prof. J. H. Kastle* (Univ. of Ky.), pres.—New Orleans Acad. of Science: *Dr. Gustav Mann* (Tulane Univ.), vice pres.—Assoc. Amer. Physicians: *Dr. S. J. Meltzer* (Rockefeller Inst.), pres.

MEMBERS ELECT. *Nat'l Acad. of Sciences*: *Dr. F. G. Benedict*, Carnegie Nutr. Lab., Boston; *Prof. W. B. Cannon*, Harvard Univ.; *Prof. Moses Gomberg*, Univ. of Mich.

*Amer. Philosoph. Soc.*: *Dr. S. J. Meltzer*, Rockefeller Inst.; *Prof. W. A. Noyes*, Univ. of Ill.; *Prof. R. M. Pearce*, Univ. of Penn.



*Cambridge Philosoph. Soc.* (honorary members) : Prof. J. Bordet, Madame Curie, F. Czapek, Jacques Loeb.

*Miscellaneous.* Royal Bohemian Acad. of Sciences : Prof. E. G. Conklin, Princeton Univ., "foreign member."—Paris Acad. of Sciences, Sect. of Med. and Surg. : Prof. Charles Richet, Univ. of Paris to succeed Dr. J. Lucas-Championnière.—Royal Soc. of London : Prof. D. N. Paton and Dr. Siegfried Ruhemann have been recommended by the Council for election to membership.—Soc. of Intern. Med. and Pediatrics, Vienna : Dr. Samuel Amberg, Otho S. A. Sprague Memor. Inst. (Chicago), "corresponding member."—Sigma Xi, Univ. of Penn. chapter : Dr. Evelyn Witmer, U. S. Food Research Lab. (Phila.), "graduate member."

**Lectures.** OSTWALD LECTURES. In continuance of the series referred to on page 334, Dr. Wolfgang Ostwald delivered lectures on *colloid chemistry* during the months of Feb. and Mar., at the Coll. of the City of N. Y. ; McGill Univ. ; Univ. of Chicago, Kansas, Nebraska, Ohio-State, Pittsburgh, and Syracuse ; and before chem. societies in Baltimore, Indianapolis, and Washington.

Just before his return to Germany, Dr. Ostwald was the guest of N. Y. chemists at a dinner at the Chemists' Club (Mar. 19). In referring to Dr. Ostwald's after-dinner address, *The Percolator* (Bull. of the Chem. Club) said, in the issue dated Apr. 18: "Prof. Ostwald concluded by demonstrating that a great name is no extinguisher of good fellowship, and that is the right thing for men of his sort to come to America. His observations were delightful and it was generally admitted that no matter how many crowd about the round table, there will always be room for him."

HARVEY LECTURES, N. Y. Acad. of Med. Feb. 14. : Recent work on the physiolog. pathology of glycosuria, J. J. R. Macleod.—Mar. 14 : The significance of the thymus glands in Graves' disease, W. S. Halsted.

PHI LAMBDA UPSILON LECTURE, Havemeyer Hall, Columbia Univ. May 8 : Sources and manufacture of perfumes, Dr. Alois von Isakovics.

CHARLES F. CHANDLER LECTURE, on indust. chem., Havemeyer Hall, Columbia Univ., May 29 : Some aspects of indust. chem., Dr. L. H. Baekeland. (See *Science*, xl, p. 179.)



*Miscellaneous.* Prof. C. R. Bardeen, Univ. of Wis.: Feb. 18, annual address before the Univ. of Iowa chapter of Sigma Xi, on The effect of physical and chemical agents on development.—Dr. Alexis Carrel, Rockefeller Inst.: Apr. 1, 8th lecture before the Rush Soc., Phila., on Permanent active life of the tissues outside the organism.—Prof. R. G. Harrison, Yale Univ.: Jan. 29, before the Soc. for Biol. Research, Univ. of Pittsburgh, on The life of tissues outside the organism.—Prof. F. G. Hopkins, Cambridge Univ.: Oliver-Sharpey lectures, at the Royal Coll. of Physicians, London, on Disturbances in the chemical reactions of the blood.—Prof. F. E. Lloyd, McGill Univ.: April 4, before the Royal Can. Inst., of Toronto, on The artificial ripening of fruit; April 14, before the Clin. Soc. of the Western Hosp. of Montreal, on Colloids and the ultra-microscope.—Dr. Oswald Schreiner, U. S. Bur. of Soils: Feb. 11, before the Sect. of Physics and Chem., Franklin Inst., Phila., on The biochemistry of soil fertility.—Prof. C. H. Shattuck, Forestry Dep't, Univ. of Idaho: March 28, before the Puget Sound Branch, Amer. Chem. Soc., on Wood processing.

**Buildings, funds and endowments.** BUILDINGS. A new lab. building at the *Marine Biol. Lab.*, Woods Hole, Mass., was dedicated, July 10, with appropriate ceremonies.

The School of Physiol., presented to the *Univ. of Cambridge* by the Drapers' Co., was opened by Prince Arthur of Connaught, June 9. The cost of the building, with the contribution made by the company towards its equipment, has amounted to £23,500.

*Beth Israel Hosp.* has bought a new site at 16th St. and Stuyvesant Place, N. Y. City, where its new building will be erected. The new hospital will be fifteen stories high, with ample space for the lab. dep't. The cost of the new building will be about \$1,000,000.

**FUNDS.** *Carnegie grants.* The report of the pres. of the Carnegie Inst., for the year ending Oct. 31, 1913, contains the following summary of "minor grants" for research in "*chemistry*": S. F. Acree, \$2,000; G. P. Baxter, \$1,500; T. B. Osborne and L. B. Mendel, \$15,000; H. C. Jones, \$3,200; H. N. Morse, \$4,000; A. A. Noyes, \$3,000; T. W. Richards, \$3,000; H. C. Sherman, \$1,200. In "*nutrition*": Carl Tigerstedt, \$1,000. In "*physiology*": Eliza-

beth Cooke, \$1,900; E. T. Reichert, \$1,500. The amount allotted to the Nutr. Lab., in Boston, was \$46,549. The total expenditure for the year 1912-1913, in the form of grants directly in support of research, was \$969,502.72. (The pres. report was published in *Science*: 1914, xxxix, p. 225.)

*Koch grants.* The Robert Koch Foundation, at Berlin, for Research on Tuberculosis, has granted a subsidy of \$500 to Prof. *Lexer* (Jena), for research on the action of light on tuberculous tissue, and to Prof. *Kayserling* (Berlin), for roentgenologic investigation of the distribution and extent of the infection in tuberculosis-ridden families.

*Miscellaneous grants.* The Russian minister of public instruction has granted \$50,000 to the St. Petersburg Acad. of Sciences to assist it in its search for radio-active minerals throughout the Russian Empire.—The C. M. Warren Committee of the Amer. Acad. of Arts and Sciences has granted \$200 to Prof. S. Lawrence Bigelow, Univ. of Michigan, for the promotion of his study of osmotic membranes, especially those of a metallic nature.

**ENDOWMENTS.** The Univ. of Aberdeen has received \$25,000 from Lord Strathcona for the creation of a chair of agric.

Mr. R. B. Mellon, of Pittsburgh, has endowed a fellowship in internal med. in the Sch. of Med., Univ. of Pittsburgh. The fellow will be a resident of a Pittsburgh hospital and will work directly under the prof. of med., Dr. J. D. Heard. In addition, Mr. Mellon has provided funds for the purchase and maintenance of an electrocardiograph apparatus.

The board of governors of the Gen. Memor. Hosp., N. Y. City, have voted to enter into an affiliation with Cornell Univ. Med. Coll. for the conduct of the Gen. Mem. Hosp. as an institution for the study and treatment of cancer and allied diseases. This affiliation is rendered possible by the gift of a large sum from Dr. James Douglas which, in addition to the present endowment of the institution, will render the hospital largely independent of an income from other sources.

**Miscellaneous general items.** **LEAVES OF ABSENCE.** Dr. *Paul J. Hanzlik* (dep't of pharmacol., West. Reserve Univ.) has been abroad since Jan. 1st. He is working in Prof. Hans Meyer's lab.

of pharmacol. (Vienna) and incidentally visiting various laboratories in Europe. He will return in Sept.—Dr. *F. H. Scott* (dep't of physiol., Univ. of Minn.), has been granted leave of absence for the first semester of 1914-'15.

INTERNAT'L JOINT COMMISS. Prof. G. C. Whipple (Harvard Univ.) has been chosen one of three Amer. engineers to act with three Can. engineers to advise with the Internat. Joint. Commiss. on matters pertaining to the pollution of the Great Lakes.

ANOTHER MED. SCH. OPEN TO WOMEN. The trustees of the Univ. of Penn. have voted to admit women to the Sch. of Med., beginning in the fall of 1914.

"NELA." Dr. E. P. Hyde, direc. of the physical lab., Nat'l Elec. Lamp Assoc., announces that hereafter the lab. will be known as *Nela Research Lab.*, Nat'l Lamp Works of the Gen. Elec. Co., under which name its *Abstract-Bulletin* and other publications will appear.

U. S. DEP'T OF AGRIC., BUR. OF CHEM. The U. S. Dep't of Agric. has established an office in the Bur. of Chem. for the purpose of promoting a closer and more cordial cooperation among the city, state and federal *food and drug officials* of the country in the enforcement of the food and drug laws. Mr. *J. S. Abbott*, for nearly seven years dairy and food commissioner of Texas, has been appointed to this office.

Dr. *M. G. Donk*, of the Bur. of Chem., has been detailed to cooperate with the dep't of forestry, at the Univ. of Idaho, in efforts to devise better methods of utilizing mill waste and refining by-products obtained from stumps. The work will be a continuation and extension of experiments which have been conducted for the past three years by Dr. C. H. Shattuck, head of the dep't of forestry at Moscow, Idaho.

LABELING MICROSCOPE SLIDES. I now use an ordinary india ink (l'encre de chine) to which I have added a little ordinary water glass (sodium silicate sol.) such as is sold at the corner drug store for preserving eggs. It is usually better to thin, after adding the water glass, with enough water to make the ink flow freely. With this ink one can write with a fine pointed pen any label that he would have been able to write on paper. It can be put on the slide as soon as the paraffin ribbon has been mounted. If the slide was clean

when the label was written, water, alcohol and xylene may be applied to it freely without any danger of injury. Ordinary abrasion such as the slide frequently encounters in use will not in any wise affect the permanency of these labels. They can, however, be scratched off easily with a dull knife (or scrubbed off with scouring soap). A white paper label pasted on the *back* of the slide will make it even more conspicuous. LANCE BURLINGAME: *Science*, 1914, xxxix, p. 250.

GRAD. SCH. OF AGRIC. The sixth session of the Grad. Sch. of Agric., under the auspices of the Assoc. of Amer. Agric. Coll. and Exp. Stations, was held at the Coll. of Agric., Univ. of Mo. (Columbia), June 29-July 24. Among the instructors were Dr. J. Arthur Harris (biolog., Station for Exp. Evolution, Carnegie Inst., Cold Spring Harbor, L. I.); Dr. H. L. Shantz (alkali and drought-resistant plant investigations, U. S. Bur. of Plant Ind.); Prof. C. H. Eckles (prof. of dairy husbandry, Univ. of Mo.); Prof. F. B. Mumford (prof. of animal husbandry, Univ. of Mo.); Prof. H. O. Allison (assoc. prof. of animal husbandry, Univ. of Mo.); Dr. H. S. Grindley (prof. of animal nutr., Univ. of Ill.); Dr. P. F. Trowbridge (prof. of agric. chem., Univ. of Mo.)

PURE FOOD LEAGUE. An Amer. Pure Food League was organized at the N. Y. Acad. of Med., May 7, with the following officers: Pres., R. McD. Allen, chief, state food and drug dep't, Lexington, Ky.; vice pres., E. F. Ladd, state food commiss., N. D.; exec. sec'y, Alice Lakey, formerly chair. of the food commit., Nat'l Consumers' League; treas., John Martin, Board of Educ., N. Y. City. Among the names of the members of the Advis. Board, we note the following: C. L. Alsberg, chief, Bur. of Chem., Wash., D. C.; L. B. Allyn, prof. of chem., Mass. State Normal Sch., Westfield; W. M. Allen, state food chem., Raleigh, N. C.; H. E. Barnard, state food commiss., Indianapolis, Ind.; William Frear, state chem., State Coll, Pa.; Wm. J. Gies, prof. of biol. chem., Columbia Univ.; Julius Hortvet, state food chem., St. Paul, Minn.; C. D. Howard, state food chem., Concord, N. H.; W. F. Hand, state food chem., Agric. Coll., Miss.; D. R. Lucas, physician, N. Y. City; R. E. Rose, state chem., Tallahassee, Fla.; H. H. Rusby, dean, N. Y. Coll. of Pharm.; John P. Street, state food chem., New Haven, Conn.; R. E.



Stallings, state chem., Atlanta, Ga.; M. W. Jaffa, prof. of chem., Univ. of Cal.; C. D. Woods, direc., Agric. Exp. Station, Orono, Me.; E. M. Chamot, prof. of chem., Cornell Univ., Ithaca, N. Y.

## II. JOURNALS

**Amer. Jour. Physiol.** COPIES OF OFFICIAL PAPERS, WITH EDITORIAL COMMENT. *Letter addressed to the members of the Amer. Physiol. Soc.:*

Dr. W. T. Porter, who has performed a highly important service to physiology by founding, editing and being financially responsible for the *Amer. Jour. of Physiol.*, has announced his retirement from this service at the close of the current volume, the last issue of which will probably appear March first. He has generously offered to present to the Society his copyright to the name of the *Journal*.

Both the Ed. Commit. and the Council recommend the ownership and editorial control of the *Journal* by the Society. If the members approve this recommendation, the Council will at once attend to the legal necessities, and to the appointment of an editor or board of editors. The publishing of the *Journal*, under the conditions which Dr. Porter's experience has proved desirable, results in little or no financial deficit. The Council proposes, however, until other provision is made, to raise a guarantee fund to insure financial stability.

The need of arranging for the new management is urgent. You are requested, therefore, to express immediately to the Secretary (Dr. A. J. Carlson, University of Chicago) your opinion on this question: Shall the *Amer. Jour. of Physiol.* be owned by the Amer. Physiol. Soc. and edited under its control?

(Signed) W. B. Cannon, A. J. Carlson, Joseph Erlanger, F. S. Lee, S. J. Meltzer, *Members of the Council*, February 1, 1914.

*Letter addressed to subscribers for the Amer. Jour. of Physiol.:*

In 1898 Dr. W. T. Porter founded the *Amer. Jour. of Physiol.*, and during the past sixteen years he has edited and been financially responsible for it. From this wholly disinterested service, which has been of great importance to physiology, he now retires, at the completion of this thirty-third volume. Dr. Porter has generously offered to transfer his rights in the *Journal* to the Amer. Physiol.



Soc. In response to this offer the Council has voted that the Soc. continue the *Amer. Jour. of Physiol.*, and assume the ownership and editorial control. Until a permanent arrangement is made at the next annual meeting of the Soc., the business affairs of the *Journal* will be managed by the Treas., Dr. Joseph Erlanger, Washington Univ., St. Louis; and the editorial work will be in charge of the Ed. Commit., Dr. W. H. Howell, Chairman, Johns Hopkins Univ., Balt., Md.

(Signed) W. B. Cannon, A. J. Carlson, Joseph Erlanger, F. S. Lee, S. J. Meltzer, *Members of the Council of the Amer. Physiol. Soc.*, March 1, 1914.

*A second letter addressed to the members of the Amer. Physiol. Soc. on this subject:*

With but a single dissenting vote the Amer. Physiol. Soc. has decided to assume the responsibility of publishing the *Amer. Jour. of Physiol.*, and the *Journal* is now the property of the Soc. Until the permanent organization of the *Journal* shall have been effected by the Soc. at its next annual meeting, the business management of the *Journal* devolves upon the Treas. Steps must be taken at once to insure the financial success of the *Journal*, and it is obvious that in the interim, at least, the support must come largely in the form of subscriptions for the *Journal* from members of the Soc. Therefore, every member is urged to subscribe for the *Journal* and also to actively solicit subscriptions from libraries and from individuals interested in physiology, either directly or indirectly.

(Signed) Joseph Erlanger, *Treas.*, March 9, 1914.

EDITORIAL COMMENT. It is announced that Dr. W. T. Porter is to retire as editor of the *Amer. Jour. of Physiol.* at the completion of the current, thirty-third, volume of this important publication. It was largely through his initiative that this periodical was founded in 1898; and though the enterprise has received the sanction and official support of the Amer. Physiol. Soc., from the beginning, Dr. Porter not only has assumed the burden of editorial management, but also has been financially responsible for it. This wholly disinterested service has been of great importance to physiology in general, and of peculiar helpfulness to the progress of the science in America. The possibilities in the way of publication which have

been opened to the research workers in American laboratories through the inauguration in this country of journals devoted to the pre-medical sciences, can be fully appreciated only by those who little more than a decade ago were forced either to send their contributions to publications abroad, often to be printed in a foreign language, or to accept the meager opportunities offered by a few of our own medical journals. Even more important, however, is the influence that the *Amer. Jour. of Physiol.* has exerted in all parts of the educated world in enhancing the prestige of American physiologists and their work. Its high standard of excellence in form and content forced attention to the research work being accomplished here and speedily placed the rapidly developing American laboratories in the front rank. The enumeration of the prominent contributions which have appeared in the pages of the *Journal* since 1898 would unfold the story of many of the most notable advances that physiology has experienced within this period. Few who have not experienced the demands which unceasing editorial duties make on the energy and initiative, the ingenuity and forbearance, of an otherwise engaged individual, can adequately appreciate the splendid ability with which Dr. Porter so generously and willingly undertook and carried this task to the point at which the work cannot easily fail to be sustained for the future. He richly deserves the thanks of those who have the best interests of the thriving science of physiology at heart. We are glad to learn that the Amer. Physiol. Soc. will assume the ownership and editorial control, and continue the publication. Until a permanent arrangement is made, the editorial work will be in charge of an editorial committee, of which Prof. W. H. Howell of Baltimore is chairman. (*Editorial: Jour. Amer. Med. Assoc.*, 1914, lxii, p. 939.)

**Jour. Biol. Chem.** The following "announcement" appears on page 1 of the June issue of the *Jour. Biol. Chem.* (Vol. xviii, no. 1) :

The *Jour. of Biol. Chem.* enters upon its eighteenth volume with the present issue and the directors of the *Journal* take this occasion to make the following announcement: Up to the present time the work of both editing and publishing the *Journal* has been done by the board of editors appointed by the directors. The rapid growth of the *Journal* has been associated with a corresponding large in-

crease in the necessary labor of its production. After mature consideration it appeared that the objects for which the *Journal* was established would be best served if arrangements could be made for transferring part of the business of publication to an efficient organization with existing facilities for the conduct of such work. The directors take pleasure in announcing that an arrangement has been consummated by which the Rockefeller Inst. for Med. Research, an organization with which the founder of the *Journal* was closely affiliated, will undertake for them the work of publishing the *Journal*. At the same time the corporate ownership and editorial management of the *Journal* remain unchanged. It is confidently believed that the future development and stability of the *Journal* will be materially advanced by this arrangement. With the present issue Dr. Donald D. Van Slyke joins the board of editors, and the directors are confident that this appointment will add to the strength of the *Journal*. No change is contemplated in the editorial policy of the *Journal*, which will be conducted as heretofore solely with the object of providing a medium for the prompt publication of researches in every branch of biochemistry.

(Besides the addition of Dr. Van Slyke to the board of editors, referred to above, the name of Dr. W. A. Jacobs, Rockefeller Inst., appears on the list of collaborators. Beginning with the February issue, the name of Dr. Henry L. Wheeler no longer appears among those of the collaborators.)

**Int. Zeit. f. physik.-chem. Biol.** Prof. J. Traube (Charlottenburg-Berlin) is the editor, and Drs. H. J. Hamburger (Groningen), V. Henri (Paris) and Jacques Loeb (N. Y.) the associate editors, of a new journal entitled *Internationale Zeitschrift für physikalisch-chemische Biologie*. Price per vol., 15 Marks (about three vol. a year). Publisher: Wilhelm Engelmann, Leipzig and Berlin.

**Engler's Botan. Jahrbuch.** Prof. Adolph Engler, direc. of the Royal Botanic Garden and Museum, at Dahlem near Berlin, celebrated his 70th birthday on March 25th. He was presented with his life-size marble bust and a copy of the *Fest-Band of Engler's Botan. Jahrbücher*, containing forty illustrated contributions, largely from his pupils.

**Münchener med. Wochenschr.** A recent number of this jour-

nal is a special issue in honor of the sixtieth birthday of Prof. Paul Ehrlich, which occurred on Mar. 14.

### III. INSTITUTES

**Proposed Internat. Chem. Inst.** The recent foundation, with exceptional rapidity and unanimity, of the Internat. Assoc. of Chem. Soc. shows that chemistry, as a science, has advanced to a position where unregulated individual efforts are no longer sufficient and must be replaced by organizing the efforts of all chemists. Such possible and necessary undertakings of general value discussed in the proceedings were: (1) Uniformity of nomenclature of chemic substances; (2) inclusion of the internat. commit. on atomic weights in the Assoc. of Chem. Soc.; (3) uniformity in the nomenclature of physic and chemic constants; (4) conformity in the editing of tables of contents of chemic publications; (5) standardization of the writing of abstracts and other reviews of new publications in chemistry; (6) preparation of an internat. auxiliary language for publications of universal interest; (7) standardization of the size of publications; (8) arrangements for limiting the printing of an article in different publications; (9) preparation of a chemic thesaurus in which the gist of all chemic knowledge will be presented in a clear and trustworthy manner. (WILHELM OSTWALD: *Science*, 1914, xl, p. 147.)

**Russell Sage Inst. of Pathol.** At a meeting of the board of directors of the Russell Sage Inst. of Pathol., held in New York, June 5, the following officers were elected: Pres., *D. Bryson Delaven*; vice-pres., *Simon Flexner*; sec., *T. C. Janeway*; treas., *Graham Lusk*. Appointments to the scientific staff: Scientific direc., *Graham Lusk*; med. direc., *Eugene F. Du Bois*; chemist, *F. C. Gephart*, assis., *A. L. Meyer*.

**Radium Inst. of Amer.** The work of the Radium Inst. of Amer. was inaugurated at a public meeting in Fayerweather Hall, Columbia Univ., Feb. 17, at which Prof. Nicholas Murray Butler presided. *Scientific program*.—Introductory remarks: *President Butler*.—The experiment of counting the alpha particles: Prof. *Geo. B. Pegram*.—Some experiments with radium emanation: Prof. *William Duane*.—Therapeutic use of radium: Dr. *Robert Abbe*.—Some



biological effects from radium: Prof. *F. C. Wood*. The names of the officers of the Inst. follow: Pres., Prof. *Nicholas Murray Butler*; 1st vice-pres., Provost *Edgar F. Smith*; 2d vice-pres., Dr. *Robert Abbe*; treas., Dr. *Hugo Lieber*; sec'y, Prof. *Geo. B. Pegram*. Board of directors: the officers, and Dr. *C. F. Chandler* (chair.), Prof. *Bergen Davis*, Prof. *Wm. J. Gies*, Mr. *Ellwood Hendrick*, Dr. *Willy Meyer* and Dr. *Hugo Schweitzer*.

**Leegen Inst. for Physiology.** By the *bequest* of \$300,000, under the will of the late Prof. Leegen, a former member of the Vienna med. faculty, the Acad. of Sciences of Vienna has obtained means to erect a *special institute for physiology*. The idea is to devote the institute wholly to scientific research, no beginners to be admitted, and the men working there to be appointed as "whole-time" officers, who may *not* devote their time to any other office. The Acad. has also obtained control of the Vienna Biol. Inst., together with a large endowment to keep it going. From this Inst. emanated the biological discoveries by Drs. Kammerer and Pribram, and now, in connection with the *Leegen Inst.*, exp. physiol. on a large scale, for purely scientific purposes, will be possible in Vienna, apart from the research in progress in the univ. laboratories.

**Kaiser Wilhelm Inst. for the Physiol. of Work.** An Inst. devoted to the physiology of work is being erected under the auspices of the Kaiser Wilhelm Soc. for the Adv. of Science. Prof. Rubner has been appointed direc. and will have three assis., one for physiol. chem. and metabolism, one for exp. physiol. and psychol., and one for statistical and economic studies. The purpose of the Inst. is to obtain exact data regarding human effort of a physical and intellectual nature, both in general and with reference to special conditions in childhood, youth and old age, and in various conditions and for different races.

**Lister Inst.** Arrangements have nearly been completed for the establishment, as a memorial to Lord Lister in Edinburgh, of a Lister Inst. It is proposed that the Inst., which will be devoted mainly to research in bacteriol. and pathol., shall work in connection with the Univ., but that it shall be managed by an independent board consisting of representatives of the Royal Coll. of Phys. and Surg. and of the Univ., and probably of the Carnegie trustees, who have



recently become interested in the Lab. of the Royal Coll. It is intended that certain facilities for teaching shall also be provided. Eventually all pathol. work, both in research and teaching, in Edinburgh will probably be under the general supervision of the prof. of pathol., who, in addition to holding that chair and taking an appropriate share in the conduct of the new Inst., will act as honorary pathol. to the Royal Infirm.

**Inst. for Heredity.** The Mendelian Soc. of Vienna has celebrated the thirtieth anniversary of Mendel's death by opening a new Inst. devoted to research in heredity.

#### IV. WAR NOTES

Unavoidable delay in the issue of this number of the BULLETIN makes it possible for us to include here an indication of some of the early disturbances in science that the war in Europe has caused, and which are probably portents of the serious disorder into which active science will be thrown for years to come.

**A copy of the Secretary's announcement to the members of the Amer. Chem. Soc.:**

I regret exceedingly to be obliged to inform you that the Montreal meeting, has been indefinitely postponed, and it now seems improbable that any meeting of the Soc. will be held this fall for the reading of papers. Fortunately, comparatively little business was on the calendar, and this can be easily handled by the Directors with a possible letter ballot to the Council after the Directors have met in Sep.

The notices for the Montreal meeting were already printed and inserted in addressed envelopes ready for mailing when Pres. Richards wired to postpone mailing pending conference with the Commit. in Montreal, as the European war had just become a reality and Montreal was more or less involved. Several telegrams passed, and the following letter from Prof. R. F. Ruttan, Chair. of the Commit., explains the final decision better than any words of my own can do:

DEAR DR. PARSONS:

The declaration of war between Germany and England, found me at Metis Beach, 500 miles down the St. Lawrence, playing golf with a

<sup>2</sup> The "Montreal meeting" was to have been held from Sept. 15 to 18, inclusive.

feeling of relief that our organization for the meeting was so complete.

My first wire to you was mis-sent by a habitant operator, who did not think the order of initials was of any importance. I am very sorry for the delay. I took the first train back to Montreal, arrived this morning, and wired you.

We had a meeting of all the Exec. Commit. in town this afternoon, and with profound regret, fully realizing what it meant to you and the Soc., decided that the meeting could not be made to go in British territory this autumn. I wired you at once.

"Canada is sending the first contingent of 20,000 very soon and a second and third will follow.

Montrealers feel that we are at war with Germany and Austria, and are behaving as if the enemy were threatening us.

The Harbor, canals, etc., are under Martial Law. The excursions were off, as the company cancelled our contract, for the steamers for the rapids and harbor.

No German member of the Soc. would naturally come to British soil and all with German names would be questioned at the boundary. Many are even now turned back. We felt that the exclusion of so many prominent members of the Soc. was a high price to pay for a meeting here.

Any foreigners would be subjected to disagreeable formalities and conditions on coming here just now.

It would be impossible to attract to the Convention the slightest public interest in Montreal, outside a few dozen chemists. No one would come to the *Conversazione* or the Garden parties we had arranged, and while there would surely be the feeling of good fellowship among ourselves, it would be overshadowed by the tragic war we are in at present.

It is sad to look over the wreck of our hopes of a big and successful meeting.

Everything was organized and under way even to rehearsing for the Smoker. The toastmaster and speakers for the banquet, the chemical and other scientific "stunts" for the *Conversazione* were arranged, the hall for the exhibits prepared, which, by the way, would have been of exceptional interest. We feel very sad about it all to-day I assure you.

The Principal, Vice Principal and Sir Wm. Osler, who had promised to speak at the banquet, are in Europe, as well as many of

our staff. Their return is uncertain. Everything was against the meeting and only our desire to give you the hand of good fellowship and the advanced state of the preparations made us hesitate at all about calling everything off.

I hope you appreciate our situation and that we have your sympathy.

I came up this morning feeling sure the meeting would go, but have been convinced it could not be made more than an apology for a Convention, which it would be a waste of time to attend.

When things settle down again we will once more extend you an invitation, and hope you will do us the honor of accepting it.

I am, with kindest regards,

Sincerely yours,

[Signed] R. F. RUTTAN.

On receipt of this letter, Pres. Richards of course determined at once to call off the meeting. Quick action being necessary a letter was sent from this office simply to the Directors, to the Editors, and to the Chairmen of Divisions asking their opinion as to the desirability of attempting to hold another meeting at some resort in Sept. or perhaps later in the fall. The majority of these have now replied and the almost unanimous opinion appears to be that it will be impossible to arrange for a successful meeting early in the fall and that business conditions throughout the country render it improbable that it would be advisable to have a meeting later in the year. This latter point, however, will be definitely decided later and the *members should watch the Oct. and Nov. journals for any notice that may become necessary regarding this matter.* The present outlook is that the next meeting of the Amer. Chem. Soc. will be in New Orleans, Apr. 1 to 3, 1915.

(Signed) CHARLES L. PARSONS, *Secretary*, Aug. 15, 1914

**Dearth in the supply of potassium salts.** Outside of Germany there is no known commercial supply of potassium salts. If the German supplies are cut off during the European war, the agricultural world must either go without potassium salts after the meager supply now on hand is exhausted or bestir itself to find another adequate source of supply. Already many inquiries regard-

ing potassium salts have been addressed to the U. S. Geol. Survey, and the fertilizer journals report that small quantities of spot material are changing hands at sharp premiums. The situation is undoubtedly more acute than it was a few years ago, when national interest was first awakened to the fact that the U. S. is entirely dependent on Germany for this important class of fertilizer materials. Potassium salts are employed in many industries other than the fertilizer industry. A large amount is used in glass and soap making, and in the manufacture of a number of chem. products. These include potassium hydroxid, and the carbonate and bicarbonate, used principally in glass and soap making; potassium alums; cyanids, including potassium cyanid, potassium ferrocyanid, and potassium ferricyanid; various bleaching chemicals, dye stuffs, explosives containing potassium nitrate, and a long list of general chemicals. The imports of potassium salts, listed as such in the reports of the Bur. of Foreign and Domestic Com., include the carbonate, cyanid, chlorid, nitrate and sulfate, "caustic potash," and other potassium compounds. The importation of the above named salts, in round numbers the last three years, has averaged 635,000,000 pounds in quantity and \$11,000,000 in value. These figures represent, however, only a portion of the potassium salts entering the U. S.; they do not include the imports of kainite and manure salts used in fertilizers. The quantity of this class of materials imported for consumption in the U. S. during the last three years has averaged annually about 700,000 tons, valued at \$4,300,000. The annual importations of potassium salts have exceeded the value of \$15,000,000.

**Miscellaneous.** THE WAR AND THE MEDICAL PRESS. An evidence of one effect of the war is the small size of our British exchanges. This might be expected for no other reason than the lack of material for publication. The *British Med. Jour.*, however, in its issue for Aug. 15, gives as another reason the shortage of paper, which it states has become a very serious difficulty for the periodical press. The *British Med. Jour.* has omitted entirely its epitome of current med. lit. because it has received no German, Austrian or Russian exchanges for the previous two weeks, and very few from France. In addition to the difficulty in securing paper, because of



irregular sailing of the ships, the consumption of paper by the newspapers has increased enormously because of the demand for extra editions. The Journal has received practically no German, Austrian or Russian publications, and but few French or Belgian periodicals, since the war began. The "Berlin letter"—mailed from Charlottenburg, July 31—arrived in Chicago Aug. 25. No Paris and Vienna letters have been received of dates subsequent to the onset of hostilities. (EDITORIAL: *Jour. Amer. Med. Assoc.*, 1914, lxiii, p. 789.)

*Kolloid-Zeitschrift*. The following notice was attached to the cover of the Sept. issue of the journal edited by Dr. Wolfgang Ostwald: Wegen militärischer Einberufung von Herausgeber und Verleger werden die Hefte der "Kolloid-Zeitschrift" in der nächsten Zeit vermutlich in etwas grösseren Abständen erscheinen.

UNIV. BUILDINGS AS ENGLISH HOSPITALS. The new buildings of the Univ. of Birmingham, at Edgbaston, have been taken over by the war office, and now form the first southern general hospital. Structural alterations have been effected with a view of making the hosp. as efficient as possible.

DEATH. Prof. B. Alfred Berthelm, member of the Georg Speyer Haus, in Frankfort a M., being drawn to join his regiment, lost his life on August 17 at Berlin, in consequence of an accident, at the age of 35 years. Besides work on alkyl combinations of thallium and on hydrates of molybdic acid, he has published numerous articles, some of them with Prof. Paul Ehrlich and Dr. Benda, on nitro- and amino-phenyl arsenic acid and their derivatives, and on *p*-amino-phenyl arsenic oxide, di-amino arsenobenzenes, and their derivatives. Professor Ehrlich writes, in the *Frankfurter Zeitung*, that to Berthelm belongs the distinction of having accomplished the synthesis of salvarsan.

## V. COLUMBIA UNIVERSITY BIOCHEMICAL ASSOCIATION

### I. General notes

**Deceased.** *Hugo Kronecker*, for many years (and at the time of his death) professor of physiology at the University of Bern and director of the Physiological Institute (Hallerianum), died June 6, aged 75 years. (See pages 345 and 523.)



*Arthur Wharton Swann*, instructor in clinical medicine and in clinical pathology; assistant visiting physician to the Presbyterian Hospital, and chief of the medical clinic of the Presbyterian Dispensary; died in the Manhattan Eye, Ear and Throat Hospital, New York City, May 28, from septicemia, following an operation on the throat a week before, aged 33 years. Dr. Swann was engaged for some time in a study, in the Columbia Biochem. Lab., of possible relations between rheumatism and urinary lactic acid.

**Married.** April 23: Miss Eleanor Riehm, of Newark, N. J., and Dr. *Clayton S. Smith*.—June 18: Miss Ruth Fulton and Prof. *Stanley R. Benedict*.

**Awards of degrees.** HONORARY DEGREES. Prof. *A. R. Bliss*: M. D., Birmingham Med. Coll. (Grad. Sch. of Med., Univ. of Ala.).—Prof. *John Howland*: M.A., Yale Univ.

DEGREES IN COURSE. Prof. *Jean Broadhurst*: Ph.D., Cornell Univ. (See page 472).—Dr. *Nathan Rosenthal*: A.M., Central High Sch., Phila. Additional awards of degrees are indicated on pages 519 and 521.

**Associations and societies.** OFFICERS ELECT. Dr. *C. L. Alsberg*: member of the council on pharm. and chem., Amer. Med. Assoc.; member of the advis. board, Amer. Pure Food League.

Dr. *C. Stuart Gager*: member of the council of sect. G, Amer. Assoc. for the Adv. of Science.

Prof. *P. B. Hawk*: member of the exec. commit. and Dr. *J. S. Hepburn* of the program commit., Phila. Sect. of the Amer. Chem. Soc.

Prof. *John Howland*: member of the council on pharm. and chem., Amer. Med. Assoc.

Prof. *Wm. T. Horne*: sec.-treas., Western Amer. Phytopathol. Soc., recently organized at Davis, Cal.

Dr. *D. R. Lucas*: member of the advis. board, Amer. Pure Food League.

Dr. *C. A. Mathewson*, pres., N. Y. Assoc. of Biol. Teachers.

Prof. *R. C. Osburn*: vice-pres., N. Y. Acad. of Sciences; sec'y, Amer. Fisheries Soc.

Dr. *A. M. Pappenheimer*: pres., N. Y. Pathol. Soc.

Prof. *A. F. Shull*: member of the ex. commit., Amer. Soc. of Zool.

Prof. *Alexander Smith*: trustee of the Chemists' Club (N. Y.); representative of the Amer. Chem. Soc. on the Commit. of Graphic Representation of the Amer. Soc. of Mechan. Engineers.

Prof. *C. R. Stockard*: sec.-treas. Amer. Assoc. of Anatomists.

Dr. *Philip Van Ingen* (med. advisor of the N. Y. Milk Commit.): member of the Central Council of Public Health of the Health Fed. of the City of N. Y. This organization aims to serve as a clearing house for all ideas for the improvement of health conditions in N. Y. City.

Prof. *W. H. Welker* and Dr. *E. G. Miller, Jr.*, were among the organizers of a Med. Research Club at the Coll. of Med., Univ. of Ill. (Chicago). Prof. Welker was elected sec'y for the remainder of the college year and pres. for the ensuing year.

MEMBERS-ELECT. *Honorary membership.* Dr. *Jacques Loeb*: hon. memb. of the Cambridge Philosoph. Soc.; corresp. memb., Paris Acad. of Sciences, sect. of anat. and zool., in succession to the late Lord Avebury.

*Active membership:* Dr. *A. E. Cohn*: Amer. Soc. f. Pharm. and Exp. Therap.

Dr. *E. F. DuBois*: Amer. Physiol. Soc.

*Mabel P. Fitzgerald*: Amer. Physiol. Soc.

Dr. *H. D. Goodale*: Amer. Soc. of Zool.

Dr. *R. A. Gortner*: Amer. Soc. of Naturalists.

Dr. *Louise H. Gregory*: Amer. Soc. of Zool.

Dr. *E. C. Kendall*: Amer. Soc. Biol. Chemists.

*Sidney Liebovitz*: Chemists' Club, N. Y. (non-resident).

Dr. *H. A. Mattill*: Amer. Physiol. Soc.

Dr. *A. M. Pappenheimer*: Harvey Society.

Prof. *H. von W. Schulte*: Harvey Society.

Prof. *Wm. H. Woglom*: Harvey Society.

Prof. *Hans Zinsser*: Amer. Soc. f. Exp. Pathology.

**Appointments.**<sup>3</sup> Amer. Museum of Nat. Hist. (N. Y.): Dr. *Louis Hussakof*, curator of ichthyology (promotion).

Bellevue Hosp. (N. Y.): Dr. *O. M. Schloss*, adjunct assis. physician, children's service.

<sup>3</sup> See also pages 490 and 517.

Brooklyn Training Sch. for Teachers: Dr. *C. A. Mathewson*, head of the Science Dep't.

College of Dental and Oral Surgery of N. Y.; Dr. *H. H. Janeway*, prof. of physiol. and hygiene.

Columbia Univ.: Dr. *William Darrach*, assis. prof. of surgery (promotion); Dr. *S. W. Lambert* (recently prof. of therap.), prof. of clin. med.; Prof. *Charles C. Lieb*, assoc. prof. (and head of the dep't) of pharmacol. (promotion).—Dr. *A. W. Pappenheimer*, assis. prof. of pathol. (promotion).—Teachers' Coll.: Dr. *Jean Broadhurst*, assis. prof. of biol. (promotion).

Cornell Univ. Med. Sch.: Dr. *N. B. Foster*, assis. prof. of med.; assoc. attending physician, N. Y. Hosp. (promotion).

Iowa State Univ.: Prof. *Guy West Wilson* has been employed during the last fiscal year as an agent of the U. S. Lab. of Forest Pathol. and stationed at the Agric. Exp. Station, New Brunswick, N. J. Here he was engaged, in cooperation with Dr. M. T. Cook, in studying the relation of tannin and other cell contents of the chestnut to the blight fungus. He has been appointed to the recently created chair of Mycology and Plant Pathol. in the State University of Iowa (Iowa City), with the rank of assis. prof.

Johns Hopkins Univ.: Dr. *H. O. Mosenthal*, assoc. prof. of med.; Prof. *Edwards A. Park*, assoc. prof. of pediatrics (promotion).

Long Island Hosp. Med. Coll.: Dr. *Matthew Steel*, prof. of organic and biol. chem. (promotion).

Manhattan Ear, Eye and Throat Hosp. (N. Y. City): Dr. *J. G. Dwyer*, pathol.

Mount Sinai Hosp., N. Y. City.: Dr. *Ernst Boas* and *Nathan Rosenthal*, internes.

N. Y. City Dep't of Health: Dr. *Chas. F. Bolduan*, head of the Bur. of Public Health Education.

Presbyterian Hosp. (N. Y.): Dr. *T. F. X. Sullivan*, interne.

Rockefeller Inst.: Dr. *A. E. Cohn*, assoc. member in med. (promotion).

Russell Sage Inst. of Pathol.: Dr. *E. F. DuBois*, med. direc.

U. S. Food Research Lab. (Phila.): Dr. *E. D. Clark* (U. S. Bur. of Soils), investigator of fish and fish products.

Univ. of Bern: Prof. *Leon Asher*, prof. of physiol. (promotion).

Univ. of Ill., Coll. of Med. (Chicago): *Grover Tracy*, assis. in physiol. chem.

Univ. of Mich.: Prof. *A. F. Shull*, junior prof. of zool. (promotion.)

Univ. of Minn.: Dr. *R. A. Gortner* has resigned the position of resident investigator in biol. chem. at the Station for Exp. Evolution of the Carnegie Inst., which he had held since Sep. 1. 1909, to accept the position of assoc. prof. of soil chemistry. Dr. Gortner will be a member of the faculties of the Agric. Coll. and the Graduate Sch., and will have charge of the research on the nature of the organic matter in soils.

Univ. of Wis.: Dr. *Wm. H. Peterson*, assis. prof. of agric. chem. (promotion). Dr. Peterson is spending a leave of absence in Europe, where he has devoted three months to work with Prof. Neuberg (Berlin).

Vassar Coll. (Poughkeepsie, N. Y.): Dr. *Cora J. Beckwith*, assis. prof. of zool. (promotion).

Wells Coll. (Aurora-on-Cayuga, N. Y.): *Ruth S. Finch* (Barnard Coll., Columbia), instr. in chem.

Women's Affiliated Coll. of Del. (Newark): Dr. *Winifred J. Robinson* (Vassar Coll.), dean.

SUMMER SESSION APPOINTMENTS. Prof. *J. E. Kirkwood* is conducting the courses in botany at the summer session of the Univ. of Montana (Missoula).—Prof. *D. D. Whitney* is assoc. in compar. zool. in the "board of instruction" for the summer session at the Biol. Lab. of the Brooklyn Inst. of Arts and Sciences, at Cold Spring Harbor, L. I.—Prof. *L. L. Woodruff* is one of the summer instructors in embryology at the Marine Biol. Lab., Woods Hole, Mass.

Lectures. Prof. *John Howland* (Johns Hopkins Univ.): 7th Rush Soc. lecture, Univ. of Penn., Mar. 11, on A consideration of certain aspects of rachitis.—Dean *S. W. Lambert* (Columbia Univ.): addressed the Fed. of State Med. Boards of the U. S., Chicago, Feb. 25, on What instruction ought medical colleges to give in pharmacology?

**Miscellaneous.** The statement in *Science* (Feb. 13, p. 248) that "Dr. *Emil Abderhalden*, prof. of physiol. at the Univ. of Halle, will lecture at Columbia Univ. next autumn" was incorrect. It is probable that the rumor originated in a misunderstanding of the import of Prof. Abderhalden's election to, and acceptance of, corresponding membership in the Biochem. Assoc.

Sec. Houston, of the U. S. Dep't of Agric., has abolished the Board of Food and Drug Inspection. Appeals of the nature which formerly went to this Board will be submitted to Dr. *C. L. Alsberg*, who will be assisted by Dr. *R. L. Emerson*, of Boston.

Dr. *F. D. Fromme*, of Purdue University, made a botanical trip through Texas, New Mex. and Ariz. during the month of Feb., in order to obtain additional information on the life histories of certain species of Uredinales.

The report of the pres. of the Carnegie Inst., for the year ending Oct. 31, 1913, refers to researches by Dr. *R. A. Gortner* and Prof. *B. E. Livingston*. Regarding the work of Dr. Gortner, pres. Woodward comments in general as follows: "The importance of the biochem. lab., in charge of Dr. Gortner in connection with the dep't, has been well attested during the year by the aid he has rendered in the complex studies evidently essential to further advances in the problems of plant and animal evolution."

The Lebanon Hosp. Lab. has established a Dep't of Physiol. Chem. for the conduct of routine and research work. This department will be under the care of Drs. *M. J. Gottlieb* and *William Wooschin*.

The Carnegie Inst. expedition to Torres Straits has returned. Dr. *E. N. Harvey* was a member of the party.

The first report of an investigation that has been in progress for a year in regard to the sanitation, food and social hygiene of students has been presented by Dr. *Wm. H. McCastline*, the health officer of Columbia Univ. The report shows that there have been few cases of contagious or infectious disease and that the number of students who have been willing to come for consultation in regard to moral problems is most gratifying. It is affirmed that as a class Columbia men are of excellent principle and high moral caliber. Dr. McCastline has organized a student board of health, whose duty



it shall be to improve the eating houses and restaurants in the vicinity of the Univ. Two courses in social hygiene have been arranged, one for the freshman year, which shall cover all the facts that a young man should know in relation to personal and social hygiene, and one for the senior year which shall have for its object the presentation of facts that will enable the men to appreciate their obligations as men to society and the home. (Jour. Amer. Med. Assoc., 1914, lxii, p. 48.)

Prof. *L. B. Mendel* represented Yale at the preliminary conference in Baltimore, last Nov., which initiated a movement for the organization of a Nat'l Assoc. of Univ. Professors.

Dr. *Jacob Rosenbloom* is now giving his entire attention to diseases of metabolism, devoting much of his time to research in the West Penn. Hosp., the remainder to medical practice, in Pittsburgh, Pa.

Dr. *E. A. Spitzka* has resigned the prof. of anatomy at Jefferson Med. Coll. He plans to take up the practice, in N. Y. City, of his father, Dr. C. E. Spitzka, who died last January.

Besides Dr. *Jacques Loeb* (assoc. ed.), the collaborators for the new *Intern. Zeit. f. physik.-chem. Biologie* include the following members of the Biochem. Assoc.: *Leon Asher, Filippo Bottazzi, E. N. Harvey, A. B. Macallum, Sven Hedin* and *S. P. L. Sörensen*.

## 2. Proceedings of the Association

Abstracts of the papers comprising the scientific proceedings of the February and April meetings of the Assoc., are given on pages 454-471. The proceedings of the June meeting will be published in the next number of the *BIOCHEM. BULL.*

## 3. Columbia Biochemical Department

**Appointments from the staff.** Dr. *Walter H. Eddy* (assoc.), acting principal, N. Y. High Sch. of Commerce (Jan.-June); principal of the High School of Commerce Annex (120 W. 46th St., N. Y. City).—Dr. *Alfred P. Lothrop* (assoc.) assis. prof. of biol. chem., Queen's Univ., Kingston, Ont.—Dr. *Herman O. Mosenthal* (assoc.), assis. prof. of med., Johns Hopkins Univ.—Mr. *Arthur Knudson* (assis.), adjunct prof. of physiol. chem. and exper. pharmacol., Albany Med. Coll.—Miss *Ethel W. Wickwire* (assis.), prof.

of physiol., N. Y., Med. Coll. and Hosp. for Women.—Dr. *Charles Weisman* (assis.), sanitary chem., U. S. Public Health Service, to conduct field investigations in occupational diseases and ventilation.—Mr. *Christian Seifert* (lab. assis.), lab. assis., dep't of med., Johns Hopkins Univ.

**Resignation from the staff.** Dr. *Sergius Morgulis* (instr.) has resigned to devote all his time in this lab. to research on the metabolism of fishes under the auspices of the U. S. Bur. of Fisheries.

**Appointments to the staff.** The following appointments have been made: Dr. *Edgar G. Miller, Jr.* (recently instr. in physiol. chem., Med. Sch. of the Univ. of Ill., Chicago, formerly assis. in this lab.), associate.—Dr. *Benjamin Horowitz* (assis. prof. of physiol. chem., Med. Sch. of Fordham Univ., formerly assis. in this lab.), associate.—Dr. *Max Kahn* (lately chemist in the pharmacol. lab., U. S. Bur. of Chem., formerly assoc. in this lab.), associate. Dr. Kahn also occupies the positions of director of the chemical lab. of the Beth Israel Hosp., and chief of the dep't of internal med., outpatient dep't, Mt. Sinai Hosp., N. Y. City.—Dr. *William Weinberger* (sometime assis. in this lab.), associate. Dr. Weinberger also holds the position of adjunct attending physician, Lebanon Hosp., N. Y. City.—Mr. *Arthur D. Emmett* (assis. chief, animal nutr., Agric. Exp. Station, Univ. of Ill.), instructor.—*Hattie L. Heft*, assistant.—*Robert Bersohn*, assistant.—*James Lyons*, *Charles Bogin* and *Abraham K. Yonans*, lab. assistants.

**Comment on the changes in the personnel of the staff.** For some time during the late spring and early summer the disintegration of the staff proceeded to a degree and with a velocity that could hardly have been greater if Uncle Sam had been drawn into the war and every able bodied man "called to the colors." The three senior associates, Drs. Lothrop, Eddy and Mosenthal, whose retirement is announced in the foregoing statement, were appointed assistants in 1908 and in length of term, and effectiveness, of service, were a veritable "old guard" upon whom the efficiency of the departmental work in all its phases depended in very large degree. Those who succeed them—Drs. Miller, Horowitz, Kahn and Weinberger, and Mr. Emmett—were former officers or advanced students

*in this laboratory*, and will undoubtedly maintain the high standards of instruction and research which always characterized the work of their predecessors.

Every member of the Assoc. will learn with interest that Mr. Seifert has gone to Johns Hopkins Univ., and will wonder how we are going to get along without our veteran lab. assis. Frankly, we don't know! Chris entered the service of the lab. a few weeks after its original equipment, in the fall of 1898—sixteen years ago—and has labored hard, faithfully and with unusual efficiency ever since. Messrs. Charles Bogen and Abraham K. Yonans have been selected to succeed Chris, and if each fills *one* of his shoes we shall be well satisfied. The regret we feel that Chris's long service here has been broken by his resignation is minimized to some degree by the realization that his new environment and position will afford him the opportunities and the comforts he richly deserves. He leaves us with our cordial good wishes attending him and his family.

**Associations and societies.** OFFICERS-ELECT. H. B. Clough: treas., N. Y. Assoc. of Biol. Teachers.

F. W. Hartwell: cor. sec., N. Y. Assoc. of Biol. Teachers.

P. W. Punnett: sec., Columbia Chapter of Phi Lambda Upsilon.

MEMBERS-ELECT. Edgar Altenburg: Columbia chapter of Sigma Xi.

A. W. Buswell: Columbia chapter of Sigma Xi.

Gustav Egloff: Columbia chapters of Sigma Xi and Phi Lambda Upsilon.

H. B. Goodrich: Columbia chapter of Sigma Xi.

F. G. Goodridge: Harvey Society.

Paul E. Howe: Harvey Society.

Arthur Knudson: Columbia chapter of Phi Lambda Upsilon.

H. J. Muller: Columbia chapter of Sigma XI.

A. P. Tanberg: Columbia chapter of Phi Lambda Upsilon.

P. W. Punnett: Columbia chapter of Sigma Xi.

**Awards of higher degrees at Columbia to students of biolog. chem.** DOCTORS OF PHILOSOPHY. Of the twenty recipients of the degree of Ph.D. under the Fac. of Pure Science, at Columbia's last commencement, ten had taken "majors or minors," or both (or "extra" courses) in the Biochem. Dep't. The names of the can-

didates, and the subjects of their major and minor courses, are given below :

Name of candidate.	Major.	Minor.	Minor.
Cora J. Beckwith	zoology	zoology	{ biological chemistry physiology
Sidney Born	chemistry	chemistry	biological chemistry
R. P. Calvert	chemistry	chemistry	biological chemistry
D. J. Edwards <sup>1</sup>	physiology	zoology	physiology
Fred D. Fromme <sup>1</sup>	botany	botany	bacteriology
Mildred A. Hoge	zoology	zoology	{ biological chemistry zoology
Marguerite T. Lee	biological chemistry	zoology	education
V. E. Levine	biological chemistry	biological chemistry	{ pharmacology education
Charles Packard	zoology	zoology	biological chemistry
E. L. Scott	physiology	{ biological chemistry istry	{ chemistry botany

**MASTERS OF ARTS.** The A.M. degree was recently conferred upon the following advanced students in the Biochem. Dep't: Robert Bersohn, *Kate Field*, H. B. Goodrich, *Helen Gavin*, *Greta Gray*, *Helen M. Hahn*, *Margaret F. Kelley*, I. J. Kligler, Walter M. Kraus, *Grace MacLeod*, Wm. A. Perlzweig, *Ethel Ronzone*, Jacob Shulansky, *Margaret B. Stanton*, Arthur W. S. Thomas, *Jennie A. Walker*, Alexander Weinstein, *Ethel W. Wickwire*.

**DOCTORS OF PHARMACY.** The following students of biolog. chem. at the Sch. of Pharmacy received the degree of Phar.D.: E. B. Ackerman, Rafael Cabrera, R. L. Flett, Pasquale Guerrieri, Henshaw Jee, A. J. A. Traub, J. H. Wiener.

**Summer session. COURSES.** The dep't is conducting six courses in nutrition, biochem. methods, and research at the summer session now in progress at Columbia (July 6-Aug. 14). Two of these courses are given at Teachers Coll., by Prof. Gies, Dr. Emily C. Seaman and Miss Tula L. Harkey; four are given at the Coll. of Phys. and Surg., by Prof. Gies and Mr. W. A. Perlzweig. The biochem. lab. at the Med. Sch. is open daily for research and will continue so all summer.

*Course of research in dental chem.* One of the courses consists of research in dental chem.—the first formal course ever offered

<sup>1</sup> Took "extra" courses in biological chemistry.



anywhere in this subject. The names of the students taking it are: Louise C. Ball, Leon Loewe, Arnold Messing, Wm. A. Perlzweig and G. H. Whiteford—all candidates for the M.A. or Ph.D. degree. The work in progress relates to saliva and tooth enamel, and consists of studies of (a) reaction and turbidity of saliva, (b) tests for sulfocyanate, glucose and glycogen in saliva, (c) properties of salivary mucin, (d) effects of sugar on salivary secretion, (e) nutritional (?) changes in enamel, (f) effects of putrefactive products and ferric chlorid on enamel, (g) solvent action of carbon dioxide, mucin, alkali phosphates and bicarbonates on tri-basic calcium phosphate. Valuable results are accumulating and will be published in the Sept. issue of the *Jour. of the Allied Dental Soc.*

INVESTIGATORS. The workers named below have been engaged in research, in the biochem. lab. at the Med. Sch., at various times during the vacation:

Louise C. Ball, Louis Berman, Robert Bersohn, O. C. Bowes, William J. Gies, Frederic G. Goodridge, Hattie L. Heft, Benjamin Horowitz, I. J. Kligler, Arthur Knudson, Victor C. Levine, Leon Loewe, Alfred P. Lothrop, Arnold Messing, Herman O. Mosenthal, Sergius Morgulis, William A. Perlzweig, Louis Pine, J. Rockman, Oscar M. Schloss, M. K. Thornton, William Weinberger, Charles Weisman, G. H. Whiteford.

**Miscellaneous items.** Prof. Gies is a member of the Advis. Board of the recently organized Amer. Pure Food League; of the Advis. Council to the N. Y. City Board of Health, and of its sub-commit. on food inspection; and of the Board of Direc. of the Radium Inst. of Amer. The degree of Doctor of Science was conferred upon him by Gettysburg Coll. at the last commencement.

Percy W. Punnett has been appointed a Univ. fellow in Chem. (1914-'15); Arthur P. Tanberg, alternate fellow in chem.; Hubert B. Goodrich, alternate fellow in zool.

On Feb. 13, Prof. Gies addressed the N. Y. Assoc. of Biol. Teachers, in Brooklyn, on Recent advances in chemical biology. He was a guest and speaker at the 15th annual dinner of the Alumni Assoc. of the Coll. of Dental and Oral Surg. of N. Y., at the Hotel Manhattan, on April 4; also at the 1st annual dinner of the Bronx Co. Dental Soc., at the Schnorer Club, on April 21. He



opened discussions of dental papers at the N. Y. Acad. of Med., on Mar. 2d, and at the Acad. of Stomatol., in Phila., on Mar. 28. On May 15th, he presented at Albany, at the 46th annual meeting of the Dental Soc. of the State of N. Y., a report of research by Dr. Morgulis and himself, on The influence of internal secretions upon the development and condition of the teeth.

Dr. V. E. Levine (assis.) has been performing the duties of head of the science dep't in the Eron School (N. Y. City) and will also serve as instructor in organic chem., in the Fordham Univ. Sch. of Pharmacy.





PROFESSORS KRONECKER AND ASHER, AND SOME OF THEIR PUPILS,  
IN THE PHYSIOLOGICAL INSTITUTE, BERN; JULY, 1899.

Standing: Professor Asher, Gies, Busch, Mühlberg. Seated: Arnold, Professor Kronecker, Esslemont.

## EDITORIALS

News of the sudden death of Professor Kronecker came as a violent shock to his friends and admirers in the Biochemical Association, but to none more so than to the writer,

**Hugo Kronecker** who has been his grateful pupil, and who enjoyed his friendship, since a memorable summer in Bern, fifteen years ago.

Professor Kronecker was a kind, gracious, sympathetic, generous and stimulating teacher. Active and enthusiastic in high degree, Kronecker set an example, in industry in research and in devotion to truth, that has inspired his many pupils the world over. He aroused the spirit of research as few teaching investigators can and, by his attitude of generous fairness to his pupils, he showed that he was far more concerned about the promotion of science than about the professional advancement of Hugo Kronecker. He was not of that cheap and all too common species of "leading scientific men" that regard their pupils as apprentices whose industry and fidelity are merely so much energy and ability for exploitation to the professional and selfish aggrandisement of "the chief." Kronecker aimed to help his pupils to stand on their own feet, but he refused to "use" them in any sense of the word. This was the never-to-be-forgotten impression that Hugo Kronecker made upon those of his pupils whose faces are pictured with his and our beloved Professor Asher's on the opposite page—an impression which one of these pupils recorded briefly but affectionately eleven years ago in the following note, in a paper by him describing work done under Kronecker's personal direction: "Throughout practically all of our research, Professor Kronecker not only directed the work, but did a very large share of it. His well-known generosity to his pupils is again shown by his desire that this investigation, which was chiefly his, shall seem to be wholly mine."<sup>1</sup>

Professor Kronecker endeared himself to a multitude of ardent and grateful friends. His memory will ever live in the hearts of all who loved him. His great influence on the advancement of sci-

<sup>1</sup> *American Journal of Physiology*, 1903, ix, p. 131.

ence will be a cumulative force in perpetuity, for his pupils and their pupils, in endless generations, will carry his spirit and his zeal into all their work.

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We are deeply indebted to Dr. Meltzer, Professor Kronecker's distinguished pupil and friend, for the appreciative biographical note regarding Professor Kronecker, which was prepared at our request and with which we are privileged to open this double number of the BULLETIN.

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From the beginning of its career, three years ago, each number of the BIOCHEMICAL BULLETIN has been unavoidably issued about a quarter after the indicated month of publication. Thus, the last **Delay in the issue** number (January) appeared in April. We began three months late and have consistently remained so. Our earnest effort to "catch up with the schedule," by issuing the April and July numbers together, in July, was defeated by an exceptional succession of unexpected incidents that enforced one exasperating delay after another. We intend, however, to take advantage of this series of mishaps by omitting the October number and beginning Vol IV with the January issue. Hereafter each volume will coincide, in periodicity, with the calendar years instead of the academic years. As we go to press (late in October), the material for the first number of the new volume is well in hand; and we are confident we shall be able to distribute the January number before the first of February, and thereafter be "on time" with each successive issue. This comment is offered in apology to our subscribers, and in explanation of a situation which has not only annoyed but embarrassed us greatly.

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In circulating blood or lymph a small amount of prothrombin is contained in solution in the plasma. This prothrombin is prevented from reacting with the calcium to form thrombin by the presence of an adequate amount of antithrombin, or, if any thrombin is formed, its coagulating effect on fibrinogen is prevented by the antithrombin. The normal fluidity of the circulating blood is dependent, therefore, upon the presence and action of the antithrombin. In blood-platelets and in



leucocytes there is contained a supply of thromboplastic material (phosphatid-compound) and also of prothrombin. On the shedding of blood the disintegration of the platelets and, to a lesser extent, of the leucocytes liberates thromboplastin and prothrombin. The former neutralizes the antithrombin, the latter, together with the prothrombin already present in the plasma, is changed to thrombin by the action of the calcium. The plasma of the circulating blood would remain unclotted when blood is shed were it not that the existing equilibrium is disturbed by the addition of the substances furnished by the disintegrated platelets. Cell-free plasmas, obtained by special means to avoid destruction of the platelets, do not coagulate spontaneously but may be made to clot by the addition of thromboplastin (kephalin).

W. H. HOWELL.

(Abstract of paper read before the National Academy of Sciences last April; presented here by the author at our request.—*Ed.*)

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Three years ago the BIOCHEMICAL BULLETIN published a paper in which the term "*lipins*" was used to designate, *collectively*, the fats and various substances, such as "lipoids," that *resemble* fats.<sup>1</sup>

**Lipins: a matter of terminology** This proposal did not include the rejection of "lipoid"; it involved merely the adoption of the term "*lipins*" to represent *conveniently* the fats and the lipoids, *i. e.*, fats and *all fat-like* substances. It was suggested, in effect, that the term "*lipins*" be used in the general way that "proteins" is commonly employed, *i. e.*, with reference primarily to convenience in description rather than to impossible accuracy in chemical characterization.

One of the recent formal adoptions of the term "*lipins*" is indicated by the following statement, among others, in *Chemical pathology*, by Prof. H. Gideon Wells (1914, 2d ed., p. 23): "Lipoids is a term in common use but of indefinite significance; most usually it comprehends the intracellular substances which are soluble in ordinary fat solvents, but which are not simple fats or fatty acids, lecithin and cholesterol being the most important of the lipoids. *For the entire group of fats and lipoids the term lipins has been pro-*

<sup>1</sup> BIOCHEMICAL BULLETIN, 1911, i, p. 51.

posed. . . . Lipoids and ordinary fats, that is, *lipins*, occur in all cells," etc.

The proposed use of "*lipins*" has been gradually increasing, evidently because of the convenience of the term. We believe that more general employment of this term would simplify current discussions of the fats and lipoids when mixtures of the two kinds of materials are concerned and when neither "fats" nor "lipoids" can convey definitely more than the accepted meaning attached to the term. To speak of fats as "lipoids" is quite as absurd as to say that starch is starch-like substance.

"*Lipins*" can be used as conveniently and more satisfactorily than the term "fat," when "*ether extract*," or "*solid matter in the ether extract*," is referred to in discussions of analytic results obtained with the Soxhlet or other extraction methods. "*Lipins*" certainly is a more suitable term than "lipoids" when *mixtures* of fats and lipoids in or from tissues, cells, etc., are under discussion. The simple derivative, "*delipinize*," which we have been using freely, is far more convenient<sup>2</sup> than the phrase "*remove the fat, lipoids and similarly soluble substances*"; it is also a good substitute in chemical terminology for the less technical though nearly obsolete term "*degrease*" ("to remove the grease from"). In the terminology pertaining to enzymes, "lipases" accords perfectly with "*lipins*," the former generic term applying to enzymes capable of transforming one or more "*lipins*." "Lipolytic," "lipoclastic," "lipotropic," etc., would relate logically to such "*lipins*" as lecithin, quite as satisfactorily as to "lipins" like tributyrin.

Until we learn "everything" about the physics and chemistry of all the fats, lipoids and other fat-like materials, we shall be unable, obviously, to select terms that will exactly, completely and finally classify these substances on a strictly chemical basis. Meanwhile, "*lipins*" will be a general convenience—a term that can easily be rejected when its serviceability ends.

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The creatin content in muscle, its quantitative relation to the total muscle substance, to the body in general, and to factors which

<sup>2</sup> Bronfenbrenner and Rockman; BIOCHEMICAL BULLETIN, 1914, iii, p. 375.

may influence these relations, has been the basis for a large amount of work in the attempt to solve the problem involving the relation between the creatinin of the urine and the creatin of the muscle. The creatinin of the urine is excreted by any given individual in constant daily amounts, under the same conditions of muscular development and tonus. Creatin is a constant constituent of vertebrate muscle, which appears in the urine, on a creatin-free diet, only as a result of (or associated with) loss of tissue protein or failure to utilize carbohydrate.

The relative constancy of the creatin content in muscle has recently been verified,<sup>1</sup> the conception of species-specificity of the creatin content supported, and the direct inter-relation between the creatin of muscle and the creatinin of the urine suggested on the basis of the uniform and constant amount of creatin in muscle. A further corroboration of the idea that the urinary creatin comes from muscle creatin, and that the creatinin of the urine has the same origin, was based upon the analysis of fasting muscle and of the determination of the creatin excreted in the urine under such circumstances. Data were presented which accounted in the urine, for the greater part of the creatin lost from muscle.

The absolute species-specificity of the creatin content in muscle has recently been questioned,<sup>2</sup> on the ground that the individual variations of any one species are, in general, within the range of concentrations for the different species. While this observation diminishes the force of the deductions on the constancy of the creatin content in muscle, it does not entirely invalidate the mass of evidence which demonstrates this factor to be fairly uniform and characteristic. The solution of the problem will come with the accumulation of more data both with the old and the new,<sup>3</sup> perhaps with more accurate, methods for the determination of creatin in muscle. Attention must be given, in interpreting these data, to the state of health and the nutritive condition of the individuals used in such studies. The experiments recently reported by Folin<sup>4</sup> show at least

<sup>1</sup> Myers and Fine: *Jour. Biol. Chem.*, 1914, xiv, p. 9.

<sup>2</sup> Folin: *Jour. Biol. Chem.*, 1914, xvii, p. 483.

<sup>3</sup> Baumann: *Jour. Biol. Chem.*, 1914, xvii, p. 15; Folin, *Ibid.*, 1914, xvii, p. 475.

<sup>4</sup> Folin: *Jour. Biol. Chem.*, 1914, xvii, p. 493.

a temporary increase in the quantity of creatin present in muscle when there is an accumulation of creatin in the blood.

The significance of muscle creatin is still obscure. That it is not an essential constituent of protoplasm is evident, for invertebrates are entirely free from even traces of creatin. Invertebrate muscle contains, however, other extractives that are not characteristic of the vertebrate muscle, such as betain. The presence of creatin in vertebrate muscle may be an indication of a *type* of metabolism characteristic of vertebrates.<sup>5</sup> That creatin, or its analogue in invertebrates, is an essential structural element has been inferred, by some, from its constant presence in muscle. This fact would not, however, preclude the possibility of its being a waste product (in an intermediate stage of catabolism) that has been carried as far along the line of chemical decomposition as the muscle cells are capable of converting it, other cells dehydrating it into creatinin. Improved methods of analysis have recently shown, however, that creatinin exists in minute amounts in muscle tissue, which fact tends to assign to muscle the property of converting creatin into creatinin. Myers and Fine have observed the conversion of creatin into creatinin in autolyzing muscle, or the reverse, depending upon the relative proportions of the two substances.

Assuming that the creatin in *living* muscle is different from that in *post-mortem* muscle, and amplifying the conception of Urano, in which creatin is considered to be combined and held in muscle in some non-dialyzable form, Folin<sup>7</sup> has suggested that "living muscles contain virtually no creatin, and that the creatin found on analysis is a post-mortem product originally constituting a part of the living protoplasm." It is from this complex, Folin further concludes, that creatinin originates in normal metabolism but in unusual conditions there is "an abnormal breakdown into creatin." If this complex is the source of the creatinin of the urine, such a conception harmonizes with that relating to the diminished creatinin excretion in the urine coincident with a decreased quantity of muscular tissue. For, as the cell mass becomes less (there is probably never a com-

<sup>5</sup> Wilson: *Jour. Biol. Chem.*, 1914, xvii, p. 385.

<sup>6</sup> Myers and Fine: *Jour. Biol. Chem.*, 1914, xvii, p. 65; Folin: *Ibid.*, p. 475; Shaffer: *Ibid.*, xviii, p. 525.

<sup>7</sup> Folin: *Jour. Biol. Chem.*, 1914, xvii, p. 493.



plete disintegration of the cellular structure in the conditions under consideration) these complexes associated with the protoplasm become fewer in number and liberate smaller amounts of creatinin, or are subjected to equally diminished cellular activities.

The acceptance of the idea that the creatin which appears in the urine on a creatin-free diet is a measure of muscular disintegration has been complicated by the results of Benedict and Osterberg<sup>8</sup> in their work upon the relation between the lack of power to utilize carbohydrate and the excretion of creatin. They found the creatin elimination from a phlorhizin-diabetic dog to persist at the fasting level, instead of diminishing as might have been expected, upon the reduction of the endogenous metabolism. The creatinin excretion was unaffected, in their experiments, beyond the reduction which would have resulted alone from the loss of body tissue—a fact that supports the conception of creatinin as an index of endogenous metabolism. The origin of the creatin in this, and in fasting or its related states, remains unexplained. It is possible that the internal secretions are involved in the ability to utilize creatinin.<sup>9</sup>

The findings of Benedict and Osterberg complicate the situation with regard to an understanding of the origin of creatinin. Perhaps creatinin is a product of some uniform phase of metabolism which may or may not involve creatin directly but which produces conditions favorable for the dehydration of creatin. With so few fundamental facts one is able to build numberless theories, each of which has an element of probability.

PAUL E. HOWE.

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Biologists are divided into three camps, vitalists, mechanists, and those who sit on the boundary fence. The mechanists believe that all phenomena relating to life are attributed to the action of physical and chemical processes only. The vitalists believe that life involves something beyond and behind these. Now, those who investigate natural philosophy, or physics, are endeavoring with some fair initial success, to explain

<sup>8</sup> Benedict and Osterberg: *Jour. Biol. Chem.*, 1914, xviii, p. 18.

<sup>9</sup> Kraus: *Quart. Jour. Physiol.*, 1913, vii, p. 87; Hunter: *Ibid.*, 1914, viii, p. 11.



all physical and chemical processes in terms of positive electrons, negative electrons, and of the effects produced by these in the ether, or space devoid of matter.

If both the mechanists are right, and also the physicists, then such phenomena as heredity and memory and intelligence, and our ideas of morality and religion, and all sorts of complicated affairs are explainable in terms of positive and negative electrons and ether. *All of these speculations are really outside the domain of science, at least at present.*

It has been remarked by Poincaré that each fresh discovery in physics adds a new load on the atom. The conditions which the atoms have to explain may indeed be written down, but to do so is merely to make a complete index for all books on physics and chemistry in the widest sense.

The Zeeman effect, or separation of a single line in the spectrum by suitable magnetic fields, into two or more lines, proved conclusively that the vibrations of negative electrons in the atom are the cause of the disturbances in the ether which we know as light.

We can form a clear mental picture of the general character of the atom. *It is a miniature solar system.* The sun is replaced by the positively charged nucleus. The planets, perhaps confined to one or more definite orbits or rings, are replaced by negative electrons revolving rapidly around the nucleus. The gravitational force is replaced by the electrical attraction between the positive nucleus and negative electrons.

Bohr endeavors to account for the manner in which two hydrogen atoms form a molecule. Each atom has a nucleus of positive charge and a simple electron revolving around it. Their charges are equal and opposite. The nuclei of two such atoms repel each other. The revolving electrons of two atoms close together, if rotating in the same direction, constitute two parallel currents of electricity, and these attract one another and arrive in the same plane. It is easy to make a model on a whirling table with the nuclei on an upright rod, the electrons revolving like the governor balls of an

engine. Bohr has gone further, and conceived a similar model of a water molecule with the two nuclei of hydrogen and one nucleus of oxygen in a straight line, with ten electrons revolving in their zones around them. No doubt these suggestive schemes are somewhat speculative, but it is refreshing to find a first approximation to a dynamical scheme replacing the old unsatisfactory electrostatic atoms, which probably did not approximate to the truth. Some of the formidable organic molecules must have a complexity which it may take generations of physicists to unravel.

It has been found that when a radiant emits an alpha particle or helium nucleus, the chemical properties of the newly formed radiant differ from the old. A fresh element is formed, a different valency results, and the new radiant, relative to the old, is *two* columns to the *left* in the periodic table. The atomic number has decreased 2, and the atomic weight about 4. But when a radiant ejects a *beta* particle or electron, again there is a new radiant with different valency and chemical properties, but there is a move of *one* column to the *right* in the periodic table; a gain of one in the atomic number and no change in the atomic weight. (EVE: *Science*, 1914, xl, pp. 115-120.)

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Simple minds are contented with mystic solutions, with an illusory play of words. Men of science investigate with an open mind and are satisfied with their work, which, if slow, is certainly progressive. But the mediocre mind wishes to know everything without much trouble, and has a strange longing for prompt and safe formulas. Such men are the predestined victims of prejudice and scientific quackery. (LUGARO: *Jour. Amer. Med. Assoc.*, 1914, lxii, p. 134.)

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The man of science should be the first to admit that *science can not attain to a complete understanding of anything*. The explanation of any phenomenon only uncovers new phenomena behind it that still demand explanation, in endless succession; and such is the

essential characteristic of scientific progress. Science does not aim at ultimate explanations; and could we find them, science would be emptied of its interest to the investigator. (WILSON: *Science*, 1913, xxxvii, p. 826.)

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What is scholarship? The answer is: *The discovering, the organizing and the explaining of new facts*. Only the uninformed and unscholarly are in the habit of designating the mere diffusion of knowledge as scholarship. The man who merely reads and speaks what he reads is no scholar, nor is the man a scholar who merely requires others to study what is already known. Any nation that believes only in the diffusion of knowledge is on the road to decay. (BROWN: *Science*, 1914, xxxix, p. 587.)

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The experiment, however, is by no means a modern invention. As early as the thirteenth century Roger Bacon was proclaiming to unsympathetic scholars its soundness as an instrument for the discovery of truth. . . . Although Roger Bacon's utterances in favor of experimental science were made over three centuries before the days of his illustrious fellow countryman, Francis Bacon, and at a time when such utterances were dangerous, they were by no means the earliest expression of the experiment. Some sixteen centuries before Roger Bacon's time, Aristotle wrote in simple language an account of what is probably the *earliest recorded biological experiment*. It deals with the physiology of the senses and reads as follows: By crossing the fingers a single object under them appears to be two and yet we do not say there are two; for sight is more decisive than touch. If, however, touch were our only sense, our judgment would declare that the single object is two.

But if these are the realities of the experimental method, what are its vanities? I think the chief pitfall that besets the experimentalist is apparatus. What a strange allurements this feature of the situation has for us! . . . But if apparatus is our pitfall, we must remember that many of the pioneers in the new movement have

already demonstrated to us fundamental results by means as strikingly simple. To Loeb the problem of the universe is soluble in a finger-bowl; to Morgan in a milk-jar; and we must never forget that the importance of a result is often inversely proportional to the complication of the apparatus by which it was attained. With these examples before us, let us avoid the pitfall of bright glass and shining metal. (PARKER: *Science*, 1914, xxxix, pp. 381-384.)

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Love of knowledge, *not love of renown*, is the ideal incentive for investigation. The ideal investigator is not the man who says to himself: "I am going to become an investigator," but rather the man who becomes deeply interested in a subject and is unable to find in the literature the things he is anxious to know. He is thus forced by a desire for more knowledge to become an investigator.

*Ideal research is free research.* On the other hand, fraternal relations imply fraternal obligations. The great army of investigators is composed mainly of generals. Only a few are willing to serve in any other capacity after announcing by means of a doctor's degree, or by some scientific publication, that they have learned to walk alone. It is true that many of them were supported by the kindly hand of their teacher during this first walking exhibition and some of these never learn to walk alone; but, nevertheless, *they too often want to be generals or nothing in the army of the investigators.*

*A kind of scholarly graft which is still too common is connected with the assignment of subjects for graduate theses.* Some instructors, on meeting a problem which involves an unusual amount of drudgery, seem to regard it as legitimate to lay such a problem aside until they can find a student who will take it as a thesis subject. There is no surer way to kill all research ambition on the part of the student, nor is there a surer way to secure his permanent disrespect for the teacher and the subject.

*It is simply another expression of the ignoble spirit which leads some men to regard the young and helpless as their legitimate prey.* The teacher who does not do his best to find attractive and far reaching theses subjects for his graduate students is certainly not ideally

qualified for a position in the graduate school. *The use of graduate students to promote the interest of the teacher is simply a type of scholarly graft which we may call the promoter graft.* Moreover, it is one of the most despicable types in existence, in view of the fact that it affects those who have not yet formed strong scholarly habits. (MILLER: *Science*, 1914, xxxix, pp. 810-812.)

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Important advances in knowledge are far more likely to issue from the expert than from the inexpert in research.

*It should be esteemed one of the highest attainable objects of any institution to assist in the production of investigators whom other institutions are glad to offer desirable or superior opportunities.*

As a matter of fact and of justice it must be admitted that the aggregate of high-class work of research accomplished by the bureaus of the United States government in recent decades compares very favorably with the corresponding aggregate accomplished by educational and other establishments of our country during the same period. We who labor in the latter establishments, therefore, have no adequate reason to suppose that our reputations may be much improved by invidious reflections on the methods in science followed by men who happen to live "in Washington." *Here again it is useful to remember that we and they belong to the same species.*

There appears to be prevalent a popular fallacy to the effect that writers untrammelled by competent scholarship, but who possess verbal facility, are better qualified to expound a technical subject than those who have developed it or contributed thereto.

We need first to recognize that in its inclusive aspects research is in scope coextensive with the universe of which we form an insignificant part, but in which we are obliged to play the significant rôle of interpreters if we would make the best of our opportunities. The experience of our race has demonstrated that by study and hence by understanding of this universe the roads to progress may be found. *The methods of research are the methods of science.*



They are not of recent origin. They have undergone an evolution extending far backwards towards the era of primitive man. What is new about them is a widely general and rapidly increasing recognition of them as the most trustworthy methods man has devised for the discovery of truth and the eradication of error. Along with this recognition there has gone on, and is still going on, a gradual elimination of Homeric illusions and fallacies; so that male as well as female witches must be abandoned by all except the more atavistic, while the appellation "genius" in the singular as well as in the plural is becoming one of doubtful compliment. We are coming to understand also that while there may occur flashes of wit, and even of wisdom, from abnormal types of mind, the more effective emanations of both wit and wisdom are to be expected from normal and patiently contemplative types. And thus the more striking results of research, quite commonly in the past attributed to wizards and to genii, and still so attributed by a majority, probably, of contemporary writers for the popular press, are now understood by the thoughtful to be *products rather of industry, sanity and prolonged labor than of any superhuman faculties*. (WOODWARD: *Science*, 1914, xl, pp. 221-227.)

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Industrial chemistry has been defined as "the chemistry of dollars and cents." This rather cynical definition, in its narrower interpretation, seems to ignore entirely the far-reaching economic and civilizing influences which have been brought to life through the applications of science; it fails to do justice to the fact that the whole fabric of modern civilization becomes each day more and ever more interwoven with the endless ramifications of applied chemistry.

Fortunately, true science, contrary to other human avocations, recognizes nobody as an "authority," and is willing to change her beliefs as often as better studied facts warrant it; this difference has been the most vital cause of her never ceasing progress.

To the younger generation, surrounded with research laboratories everywhere, it may cause astonishment to learn that scarcely fifty years ago, that great benefactor of humanity, Pasteur, was still

repeating his pathetic pleadings with the French government to give him more suitable quarters than a damp, poorly lighted basement, in which he was compelled to carry on his research; and this was, then, the condition of affairs of no less a place than Paris, the same Paris that was spending, just at that time, endless millions for the building of her new Opera-Palace. Such facts should not be overlooked by those who might think that America has been too slow in fostering chemical research.

However imposing may appear the institutions founded by the Nobels, the Solvays, the Monds, the Carnegies, the Rockefellers and others, each of them is only a puny effort (compared) to what is bound to come when governments will do their full share. Fancy that if, for instance, the Rockefeller Institute is spending to good advantage about half a million dollars per annum for medical research, the chewing-gum bill of the United States alone would easily support half a dozen Rockefeller Institutes; and what a mere insignificant little trickle all these research funds amount to, if we have the courage to compare them to that powerful gushing stream of money which yearly drains the war budgets of all nations.

But most governments of the world have been run for so long almost exclusively by lawyer-politicians, that we have come to consider this as an unavoidable evil, until sometimes a large experiment of government by engineers, like the Panama Canal, opens our eyes to the fact that, after all, successful government is—first and last—a matter of efficiency, according to the principles of applied science. Was it not one of our very earliest American chemists, Benjamin Thompson, of Massachusetts, later knighted in Europe as Count Rumford, who put in shape the rather entangled administration of Bavaria, by introducing scientific methods of government?

Pasteur was right when one day exasperated by the politicians who were running his beloved France to ruin, he exclaimed: In our century, science is the soul of the prosperity of nations and the living source of all progress. Undoubtedly, the tiring daily discussions of politics seem to be our guide. Empty appearances! *What really leads us forward are a few scientific discoveries and their applications.* (BAEKELAND: *Science*, 1914, xl, pp. 179-198.)

## BOOKS RECEIVED

The BIOCHEMICAL BULLETIN promptly acknowledges the receipt of publications presented to it. Reviews are matter-of-fact statements of the nature and contents of the publications referred to, and are intended *solely to guide possible purchasers*; the wishes or expectations of publishers or donors of volumes will be disregarded, if they are incompatible with our convictions regarding the interests of our colleagues. *The sizes of the printed pages are indicated, in inches, in the appended notices.*

**Chemical pathology.** Being a discussion of general pathology from the standpoint of the chemical processes involved. By H. Gideon Wells, prof. of pathology, Univ. of Chicago and Rush Med. Coll., and Director of the Otho S. A. Sprague Memorial Inst., Chicago. 2d ed. Pp. 616— $4\frac{1}{4} \times 7$ ; \$3.25 net. W. B. Saunders Co., Phila., 1914. The second edition of this invaluable text book fully meets the expectations of those of us who have constantly used the first edition (issued in 1907). It is impossible to suggest the merits of this splendid volume in notes as brief as these without the use of superlative terms in every line of comment. Written by one who has been thoroughly trained in pathology and biological chemistry, and whose experience as a teacher and investigator of the chemical aspects of pathology has been exceptional, this volume by Wells presents in masterly manner the essentials of chemical pathology from every standpoint of importance. Practitioners of medicine, expert pathologists, laboratory workers in every medical school and institute, biological chemists everywhere, and biologists in general, will find this book of exceptional utility. A biochemical laboratory cannot be up to date without it. Gies.

**Chimie pathologique tropicale de la région Atlantique.** By G. Delgado Palacios, prof., Univ. of Caracas, Venezuela. Pp. 318— $4\frac{1}{4} \times 6\frac{3}{4}$ . Published by the author, 1914. A special treatise on feces, intoxications of intestinal origin, nutritional disturbances due to intestinal influences, and intestinal disinfection, especially from the standpoint of nutrition in the tropics. The author describes the calcareous product from feces of inhabitants of the tropics, called "carcoma fécale," which occurs in the form of granules 0.1–0.3 mm. in diameter, and contains unrobilinogen and another chromogen termed *cholérythrogène*—a name intended to suggest the origin of the new chromogen and the color of its pigment derivative. The origin, significance and properties of "carcoma fécale" and *cholérythrogène*, and their relation to yellow fever and tropical pathology, are discussed in detail. The book concludes with a section on biochemical methods of general value. The author is now in this country and may be addressed "in care of the BIOCHEMICAL BULLETIN." Gies.

**Spectrum analysis applied to biology and medicine.** By C. A. MacMunn, with a preface by F. W. Gamble, prof. of zoology, Univ. of Birmingham. Pp. 112— $3\frac{3}{4} \times 6\frac{1}{4}$ ; \$1.75 net. Longmans, Green and Co., London, 1914. This excellent book, begun and continued between attacks of serious illness, was revised, for posthumous publication, by Dr. J. H. Milroy. It contains a résumé of MacMunn's classical contributions to chromatology and presents a general view of the subject, with a very valuable bibliography in conclusion. The nine chapters deal successively with the prism, spectrum analysis and absorption—

bands; chromatology of plants and animals, pigment structure; chlorophyll in plants and animals, symbiosis; hemoglobin, components and derivatives; histohematin and myohematin; quantitative spectrum analysis, the spectrophotometer; fluorescence and phosphorescence; pigments of vertebrate and invertebrate bile, and of urine; invertebrate pigments generally. There are 21 excellent illustrations, especially of absorption spectra. Gies.

**Anesthesia.** By James T. Gwathmey, anesthetist to the N. Y. Skin and Cancer, St. Vincent, Red Cross and Columbia Hospitals, in collab. with Charles Baskerville, prof. of chemistry, Coll. of the City of N. Y. Pp. 945— $4\frac{1}{4} \times 7\frac{1}{4}$ ; \$6.00, cloth. D. Appleton and Co., New York, 1914. A superb volume. Anesthesia is given masterly treatment along the lines of its history, physiology, chemistry, utility and practice. Several of the chapters on special features of the subject are written by experienced specialists. The book is exhaustive and practical from the points of view of the anesthetist and surgeon, for it includes full consideration not only of the many methods of anesthesia and of the individual anesthetics, but also of the technic for special operations, the treatment before, during and after anesthesia, and even the medico-legal status of the anesthetist. Pharmacologists and biochemists will readily detect the hand of Prof. Baskerville, the book being notable for the thoroughness and reliability of its chemical treatment. There is an encyclopedic chapter entitled "a list of anesthetics" (pp. 688-840), which alone makes the book a necessity in every biochemical laboratory. There are special chapters on such collateral subjects as electric analgesia, sleep and resuscitation; mental influence in anesthesia; hypnosis in anesthesia. There are 253 illustrations, most of them photographic reproductions of apparatus and surgical procedures. Gies.

**Nucleic acids: Their chemical properties and physiological conduct.** By Walter Jones, prof. of physiol. chemistry, Johns Hopkins Med. Sch. Pp. 118— $4\frac{3}{8} \times 7\frac{3}{8}$ ; \$1.10 net. Longmans, Green and Co., London, 1914. (One of the *Monographs on biochemistry*.) Another invaluable presentation of available data in an important field. "The nucleic acids constitute what is possibly the best understood field of physiol. chemistry, yet . . . no treatise has yet appeared (except this) which deals exclusively with this subject. Our information must be acquired either from widely scattered and often conflicting original articles which reveal order only by the application of critical ability, or from incidental chapters of general texts which appear to have been added more for completeness than for information which they contain. Under these conditions the appearance of a special volume is rather to be expected than explained." The author treats comprehensively nuclein, nucleoprotein, nucleic acid; thymus nucleic acid; yeast nucleic acid; the metabolism of nucleic acid, pyrimidins and purins; nuclease and purinases; and purin derivatives in human urine. An appendix gives a series of practical methods. As usual with the *Monographs on biochemistry* there is a very valuable bibliography and a fine index. The first edition of this monograph will certainly be "out of print" very soon. Gies.

**The nature of enzyme action.** By W. M. Bayliss, prof. of general physiology, Univ. Coll., London. 3d ed. Pp. 180— $4\frac{3}{8} \times 7\frac{1}{2}$ ; \$1.50 net. Longmans, Green and Co., London, 1914. (One of the *Monographs on biochemistry*.) The most valuable book in English on enzymes. The author has incorporated the gist of the many recent discoveries on reversibility, on combination between



enzyme and substrate, and on anti-enzymes. The chapters on these subjects have been rewritten, for the most part, and the whole book brought up to date. Gies.

**The simpler natural bases.** By George Barger, prof. of chemistry, Royal Holloway Coll., Univ. of London. Pp. 215— $4\frac{3}{8} \times 7\frac{3}{8}$ ; \$1.80 net. Longmans, Green and Co., London, 1914. (One of the *Monographs on biochemistry*.) Treats the "basic substances of animals and plants which are of general biological interest, either because of their wide distribution, or on account of the close relationship to the proteins and phosphatides." Eight chapters deal successively with the amines derived from protein;  $\omega$ -amino-acids and other bases containing a carboxyl group; betains; cholin and allied substances; creatin, creatinin, glycoeyamin and guanidins; "adrenalin"; bases of unknown constitution; "practical chemical methods and details." Chapter VIII (pp. 116-165) is an appendix on methods for the isolation of the simple bases. Gies.

**The microscopy of drinking water.** By George C. Whipple, prof. of sanitary engineering, with a chapter on the *use of the microscope*, by J. W. M. Bunker, instr. in san. analysis, Harvard Univ. 3d ed. Pp. 409— $4 \times 6\frac{3}{4}$ ; \$4.00 net. John Wiley and Sons, N. Y., 1914. This valuable book is intended primarily to serve as a guide to the water analyst and the water-works engineer and, although "elementary in character," is very useful in the biochemical laboratory. The 19 full page plates that figure the organisms commonly found in water supplies are printed in colors, thus facilitating identifications. The author writes from the standpoint of "his conviction that the micrology of water is going to play an increasingly important part in the science of sanitation." The first part of the book has been rewritten and practically every chapter contains new and important matter. The last edition was issued in 1905. Gies.

**The microtome's vade-mecum, a handbook of the methods of microscopic anatomy.** By Arthur B. Lee. 7th ed. Pp. 526— $3\frac{7}{8} \times 6\frac{3}{4}$ ; \$4.00. P. Blakiston's Son and Co., Phila., 1913. (Last previous ed., 1905.) This well known book, again brought up to date, is a volume that every histologist and microchemist finds indispensable. The increasing importance of dyes in every avenue of biological research renders this book particularly useful in many unexpected ways in the biochemical laboratory. The title does not suggest the wealth of biochemic information which is presented in this volume. A glance at the elaborate index suggests a text book of biological chemistry. Gies.

**The source, chemistry and use of food products.** By E. H. S. Bailey, prof. of chemistry, Univ. of Kansas. Pp. 517— $4\frac{1}{8} \times 6\frac{1}{4}$ ; \$1.60 net. P. Blakiston's Son and Co., Phila., 1914. Intended for the use of students of foods in high schools and colleges. The general principles of food production, manufacture and preparation are treated in such a way as to present practical information on the nature and availability of good food. The important foods and beverages are discussed with special reference to their source; methods of preparation for the market; package, preservation and shipment; composition, nutrient value and dietetic virtue; use by different peoples. A handy volume for general use in biochemical laboratories where nutrition is a subject of formal instruction. Gies.

**Biochemic drug assay methods, with special reference to the pharmacodynamic standardization of drugs.** By Paul S. Pittenger, instr. in pharmacody-



namics, and F. E. Stewart, prof. of materia medica and botany, Medico-Chi. Coll., Phila. Pp. 158—4 × 6½; \$1.50 net. P. Blakiston's Son and Co., Phila., 1914. Laboratory manual for students of pharmacy, pharm. chemistry and medicine as well as for experts engaged in laboratories devoted to drug standardization. Represents in large part the authors' experimental research. The volume deals exclusively with drugs that cannot be standardized by direct chemical means. Methods and apparatus are effectively described. The book is profusely illustrated with representations of apparatus, curves, technic, and subjects showing effects of drugs. Gies.

**The chemistry of cattle feeding and dairying.** By J. Alan Murray, lecturer in agric. chemistry, Univ. Coll., Reading, Eng. Pp. 343—3½ × 5¾; \$1.75 net. Longmans, Green and Co., 1914. The author develops and explains the fundamental principles underlying effective control of farming operations. Although intended mainly for use in colleges of agriculture, the book is very valuable for students of food chemistry, nutrition and dietetics. The four parts treat successively of constituents of plants and animals, requirements of animals, feeding stuffs, and dairying (milk and milk products). Gies.

**Researches on irritability of plants.** By J. C. Bose, professor, Presidency Coll., Calcutta. Pp. 376—3¾ × 6½; \$2.50 net. Longmans, Green and Co., London, 1913. In this work, dealing with his researches on the irritability of plants, the author introduced new methods by which the scope of his investigation was enlarged and high degrees of accuracy attained. These procedures are fully described and illustrated. "The establishment of the unity of responsive reactions in the plant and animal, which is the subject of this work, will be found highly significant, since it is only by the study of the simpler phenomena of irritability in the vegetal organisms that we can ever expect to elucidate the more complex physiological reactions in the animal tissues." The book is divided into twenty seven chapters; it contains 190 illustrations, chiefly curves showing effects. The *special* chemical chapters relate to effects of different gases on excitability of *Mimosa* and to effects of chemical agents on the automatic pulsation of *Desdemodium gyrans*. Gies.

**The essentials of chemical physiology, for the use of students.** By W. D. Halliburton, prof. of physiology, King's Coll., London. 8th ed. Pp. 324—4 × 6½; \$1.50. Longmans, Green and Co., London, 1914. Continues to hold its place as one of the most useful and reliable laboratory manuals in physiol. chemistry. Gies.

**A textbook of experimental physiology for students of medicine.** By N. H. Alcock and F. O'B. Ellison, St Mary's Hosp. Med. Sch., Univ. of London. Pp. 139—4 × 7; \$1.50. P. Blakiston's Son and Co., Phila., 1909. The preface was written by Prof. E. H. Starling who cordially commends the book. The fundamentals of mechanical physiology are clearly and effectively illustrated. Gies.

**Festschrift zum 25-Jährigen Gedenktage der Gründung der internationalen Physiologenkongresse.** By H. J. Hamburger and Ernst Laqueur. Pp. 272—4 × 7. F. Deuticke, Wien, 1914. Historical data with a résumé of the essentials, in classified form, of the scientific proceedings of the first eight congresses. Dedicated to the ninth congress at Groningen, 1913. Gies.

**Artificial parthenogenesis and fertilization.** By Jacques Loeb, memb. of the Rockefeller Inst. Originally translated from the German by W. O. Redman King, assis. lecturer in zoology, Univ. of Leeds, Eng.; supplemented and revised by the author. Pp. 312—6¼ × 3¾; \$2.50 net. Univ. of Chicago Press, 1913.

A presentation, in the author's accustomed masterly manner, of the "methods by which the unfertilized egg can be caused to develop into an embryo and the conclusions which can be drawn concerning the mechanism by which the spermatozoon produces this effect." The voluminous mass of facts recorded and discussed by the author not only supports his theory that at least two factors are involved in this process—one ("essential") which induces a change in the *surface* of the egg; a second which is "corrective"—but also relates to such problems as the "natural death of the ovum and the prolongation of its life by fertilization; the fertilization of the egg by foreign blood and the immunity of the egg to blood of its own species; the relations between heterogeneous hybridization and artificial parthenogenesis, between fertilization and cytolysis, and between permeability and physiological efficiency of acids and bases." Gies.

**Materia medica: pharmacology: therapeutics: prescription writing.** By Walter A. Bastedo, assoc. in pharmacology and therapeutics, Columbia Univ. Pp. 602—7 × 4; \$3.50. W. B. Saunders Company, Phila., 1913.

The work is divided into three sections. *Part I* serves as a general introduction and is especially commendable for the excellent discussion of the constituents of organic drugs. *Part II* deals with the individual remedies, which are considered on Schmiedeberg's plan. The discussion of the action and uses of the cathartics is unusually practical and valuable. The forty odd pages devoted to an explanation of the action of digitalis is justified by the importance of the drug and by the great increase in our knowledge of cardiac physiology and therapeutics. The action of digitalis is discussed in an original way, which makes more easy the apprehension of the complex action of this drug. The changes in the circulation are taken up according to the action on the sinus node, the cardiac muscle, the A-V bundle, the coronary and the systemic arteries. The action on each structure is first studied separately and the combined effects are then made clear. The numerous polygraphic tracings accompanying this chapter are unusually good, but it seems unfortunate that they are not elucidated by diagrams. The section dealing with the general anesthetics is also worthy of note. *Part III*, devoted to prescription writing, is short but comprehensive. Enough Latin grammar is given to facilitate prescription writing for those who have not studied Latin. The pages devoted to practice in prescription writing will prove a boon to students and teachers. It is to be regretted that preference is given throughout the book to the apothecaries' system of weights and measures rather than to the metric system. There are, as is to be expected in a first edition, numerous typographic errors. Some of these are most unfortunate, especially the confounding of grains and grams. To add to the confusion, the grain doses are expressed in Arabic figures instead of in Roman and many of the grain fractions are written as decimals. The suggestions as to treatment are conservative and are based on laboratory research as well as on clinical experience. The author has succeeded in his attempt to emphasize the value of research, both in the laboratory and at the bedside, and he pleads for a more scientific, and therefore a simpler, therapy. Lieb.

*Lehrbuch der physiologischen Chemie in Vorlesungen. I Teil: Die organischen Nahrungsstoffe und ihr Verhalten im Zellstoffwechsel.* By Emil Abderhalden, Direktor des physiolog. Inst. der Univ. Halle A. S. 3 Aufl. Pp. 736—7¼ × 4½; M 21 brosch., M 23 gebund. Urban und Schwarzenberg, Berlin, Wien, 1914.

This well known Lehrbuch, which is indispensable in the biochem. laboratory, is no longer confined to one vol., but in its 3d ed. it appears in more than one. Lectures 1-13 of the 2d ed. (carbohydrates, lipins and proteins) have been rewritten and extended to 31 in the 3d ed. There are two additional new lectures (32-33), on hemoglobin, chlorophyll and their derivatives. This amplification has permitted the author to treat his subjects more fully, of course, and to add the essentials of the newer findings in the field covered by the volume. The lectures in the new ed. maintain their high reputation for comprehensiveness, clearness, force and interest. Part II, *Die anorganischen Nahrungsstoffe*, will probably be issued in the spring of 1914. Gies.

*A manual of bacteriology for agricultural and general science students.* By Howard S. Reed, prof. of mycology and bacteriology in the Va. Polytech. Inst.; plant pathologist and bacteriologist in the Va. Agric. Exp. Station. Pp. 179—6¼ × 4; 1.25. Ginn and Co., Boston, 1914.

An unusually concise, complete and effective manual. Presents a general course in bacteriology of particular value in technical schools, especially to students of agriculture. Includes a strong section outlining study of important fermentations caused principally by fungi. The author's extended experience has enabled him to make the manual comprehensive and practical in high degree. Presents unpublished matter and many useful suggestions for biochemists.

Gies.

*Industrial organic chemistry*; adapted for the use of manufacturers, chemists, and all interested in the utilization of organic materials in the industrial arts. 4th ed. By Samuel P. Sadtler, consulting chemist, prof. of chemistry in the Phila. Coll. of Pharmacy, former prof. of organic and indust. chemistry in the Univ. of Penn. Pp. 601—7¼ × 4½; \$5.00 net. J. P. Lippincott Co., Phila., 1912.

The general plan of this standard volume remains unchanged, but a thorough revision has been made. The space devoted to analytical processes has been increased, bibliographies have been brought up to date and statistical matter wisely adjusted to the needs of the specialist. Occupying a position, in scope, between the exhaustive special treatises and ordinary hand-books, this volume is particularly useful to biochemists working on the border between pure and applied organic chemistry. The chapters of special biochemical interest are those on the industries pertaining to fats and fatty oils, essential oils and resins, cane sugar, starch and its alteration products, fermentation, wine, distilled liquors, bread, vinegar, milk, textile fibres of vegetable and animal origin, animal tissues and their products, dyes and dyeing. For the biochemist the book is unusually valuable as a work of reference. Gies.

*Untersuchungen über Chlorophyll: Methoden und Ergebnisse.* By Richard Willstätter and Arthur Stoll, Kaiser Wilhelm Inst. für Chemie. Pp. 424—7¼ × 4½; M. 20.50. Julius Springer, Berlin, 1913.

This comprehensive volume presents unpublished data, obtained by Willstätter and his pupils in recent years, on the isolation and hydrolysis of chlorophyll and the separation and quantitative determination of its component radicals. A complete compilation and revision of the essential data of Willstätter's classical studies on chlorophyll is included, and the relationship of chlorophyll and hematin is further clarified. The volume is encyclopedic in scope and presents the methods so clearly that it may be used as a laboratory handbook on chlorophyll. That it will aid and stimulate research on chlorophyll is certain and should be studied by biochemists generally. The volume is beautifully illustrated with eleven plates, which indicate details of the crystalline and spectral characters of the products. The work on which the book is based was a monumental achievement. (*See page 229 of this volume.*) Gies.

**The elements of the science of nutrition.** By Graham Lusk, prof. of physiology, Cornell Univ. Med. Col. Second ed. Pp. 402— $6\frac{1}{2} \times 3\frac{3}{4}$ ; \$3.00 net. W. B. Saunders Co., Phila., 1909.

This widely appreciated volume, by a master of the subject in both its theoretical and practical phases, is one of the best on nutrition. We use it freely in our advanced courses, and await impatiently the appearance of the third edition. Gies.

**Nutritional physiology.** By Percy G. Stiles, assist. prof. of physiology, Simmons Col.; instr. in physiology and personal hygiene, Mass. Inst. of Tech., Boston. Pp. 271— $6 \times 3\frac{1}{2}$ ; \$1.25 net. W. B. Saunders Co., Phila., 1912.

An admirable treatment of nutrition, which is very appropriately dedicated to the author's teacher, Prof. Graham Lusk. The chemical phases of physiology are concisely though none the less effectively considered; and nutrition is presented from the *dynamic* point of view without confusion with food chemistry. A very valuable addition to the growing supply of textbooks in biological chemistry for beginners. Gies.

**Essentials of pathological chemistry, including description of the chemical methods employed in medical diagnosis.** By Victor C. Myers and Morris S. Fine, prof. and instr. in path. chemistry, respectively, at the N. Y. Post-Grad. Med. Sch. and Hosp. Reprinted from the *Post-Graduate*, 1912-13. Pp. 137— $7 \times 4$ ; \$1.25. Post Graduate (Med. Jour.), N. Y. City, 1913.

A very useful compilation of laboratory methods in the pathological chemistry of digestion and excretion, also of milk and blood, with an appendix of laboratory suggestions. The discussions are practical in guidance and broad in interpretation. The book is a very handy laboratory manual. We hope the authors will carry it through numerous revisions and extensions, as the science advances and methods multiply. Gies.

**Modern research in organic chemistry.** By F. G. Pope. Pp. 324— $6 \times 3\frac{5}{8}$ ; \$2.25 net. D. Van Nostrand Co., New York, 1913.

Restricted, with interesting historical introduction, to chapters successively on polymethylenes; terpenes and camphors; uric acid (purin) group; alkaloids; relation between color and constitution of chemical compounds; salt formation, pseudo-acids and bases; pyrones; ketens, ozonides, triphenylmethyl; and the Grignard reaction. Masterly treatment of each subject. Constitutional formulas used freely and effectively. Gies.



**An introduction to the chemistry of plant products.** By Paul Haas (lecturer on chemistry, Royal Gardens, Kew) and T. G. Hill (reader in vegetable physiology, Univ. of London). Pp. 401—4 × 7; \$2.25 net. Longmans, Green and Co., 1913.

Excellent discussion of the chemistry and biological significance of many of the most important plant constituents. Besides extended treatment of carbohydrates, lipins and proteins, chapters are devoted respectively to glucosides, tannins, pigments, nitrogenous bases (alkaloids, ptomaines, purins), colloids and enzymes. Methods of preparation, detection and quantitative determination are numerous and well described. Good *subject* index. The most valuable recent contribution of its kind to phyto-chemistry. Strongly recommended to biological chemists generally—to botanists in particular. Gies.

**Practical physiological chemistry.** By Sidney W. Cole, demonstrator of physiology, Trinity College, Cambridge. Third edition. Pp. 230—4 × 6½; 7s. 6d. net. W. Heffer & Sons, Ltd., Cambridge, Eng., 1913.

Very useful laboratory manual. Subject treated chiefly from static point of view. Practical throughout. Methods well selected. Quantitative procedures given satisfactory attention. Special emphasis laid upon Folin's micro-chemical methods of urinary analysis. Good index. See review by Walter Jones, *Jour. Amer. Chem. Soc.*, 1913, xxxv, p. 1064. Gies.

**Studies from the Rockefeller Inst. for Med. Research.** Vol. XVIII; 1914. (60 reprints.) Vol. XIX; 1914. (61 reprints.)

**Studies from the Otho S. A. Sprague Memorial Inst.** Vol. I; 1912-'13. (28 reprints.)

**Pellagra.** First progress-report of the Thompson-McFadden Pellagra Commission of the N. Y. Post-Grad. Med. Sch. and Hosp. By J. F. Siler, P. E. Garrison and W. J. MacNeal, with the collab. of A. H. Jennings, W. V. King, V. C. Myers, M. S. Fine, O. S. Hillman and others. Pp. 148—4 × 7.

**Arbeiten des medicinisch-chemischen Lab. der Kaiserlichen Universität Moskau,** 1912 and 1913. (5 reprints.)

**Collected papers from the Research Lab. of Parke, Davis and Co., Detroit, Mich.** Vol. I; 1913. (30 reprints.) Vol. II; 1914. (22 reprints.)

**Collected studies from the Bureau of Laboratories, Dep't of Health, City of N. Y.** Dr. Wm. H. Park, director. Vol. VII; 1912-'13. (55 papers, chiefly reprints.)

**Carcinoma of the thyroid in the salmonoid fishes.** By Harvey R. Gaylord and Millard C. Marsh, with the collab. of F. C. Busch and B. T. Simpson. Pp. 524—5¼ × 7¼ (55 full page plates). An investigation and experimental study conducted jointly by the Gratwick Lab. of the State Inst. for the Study of Malignant Diseases, Buffalo, N. Y., and the U. S. Bureau of Fisheries.

**E. Merck's Jahresbericht über Neuerungen auf den Gebieten der Pharmakotherapie und Pharmazie.** Vol. XXVII; 1913. Pp. 601—4 × 7. E. Merck, Darmstadt, 1914.

**Coakley's Archives.** Founded and edited by W. Byron Coakley. Vol. I, No. 1 (Apr., 1914). Pp. 27—4 × 6¾; \$4.00 per vol. Published irregularly; 61 Fifth Ave., N. Y. City.

**Collected reprints: Department of Physiology and Biochemistry, Cornell Univ. Med. Coll. (Ithaca, N. Y.).** Series IV, 1913. (19 reprints.)



## INDEX

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(I) Author index (pp. 545-548);

(II) Subject index (pp. 548-560):

*The subject index (II, p. 548), consists of two main portions:*

(A) Impersonal subjects (p. 548);

(B) Personal subjects (p. 555).

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### I. AUTHOR INDEX

The names of the authors of the leading papers, and the general subjects treated by each, may be obtained promptly from the summary of contents (pp. xi-xiv). This division of the index (I) includes not only the names of the main contributors, but also the names of accredited authors of abstracts, editorials, quotations, etc.

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## OFFICERS OF THE COLUMBIA BIOCHEMICAL DEPARTMENT

Sixteenth year: 1913-'14

OFFICIAL REGISTER, JUNE 30, 1914

- WILLIAM J. GIES: *Professor and Executive Officer*; Consulting chemist, New York Botanical Garden; Pathological chemist, First Division, Bellevue Hospital; Member of the Faculties of N. Y. Teachers College and N. Y. College of Pharmacy. [B.S., Gettysburg College, 1893, M.S., 1896, Sc.D., 1914; Ph.B., Yale University, 1894 and Ph.D., 1897. Instructor, 1898-'02; adjunct professor, 1902-'05; professor, 1905-.]
- PAUL E. HOWE: *Assistant Professor and Secretary of the Staff*. [B.S., University of Illinois, 1906; A.M., 1907 and Ph.D., 1910. Assistant professor, 1912-.]
- ALFRED P. LOTHROP: *Associate and Chairman of the Staff*. [A.B., Oberlin, 1906 and A.M., 1907; Ph.D., Columbia, 1909. Assistant, 1908-'09; instructor, 1909-'12; associate, 1912-'14.]
- EMILY C. SEAMAN: *Instructor*. [B.S., Adelphi College, 1899; A.M., Columbia, 1905 and Ph.D., 1912. Tutor, 1909-'10; instructor, 1910-.]
- WALTER H. EDDY: *Associate*. [B.S., Amherst College, 1898; A.M., Columbia, 1908 and Ph.D., 1909. Assistant, 1908-'10; associate, 1910-'14.]
- HERMAN O. MOSENTHAL: *Associate*; Assistant Attending Physician, Presbyterian Hospital; Assistant Physician, Vanderbilt Clinic; Instructor in medicine. [A.B., Columbia, 1899 and M.D., 1903. Assistant, 1908-'09; instructor, 1909-'12; associate, 1912-'14.]
- FREDERIC G. GOODRIDGE: *Instructor*. [A.B., Harvard University, 1897; M.D., Columbia, 1901. Assistant, 1912-'13; instructor, 1913-.]
- SERGIVS MORGULIS: *Instructor*. [A.M., Columbia, 1907; Ph.D., Harvard University, 1910. Instructor, 1913-'14.]
- ARTHUR KNUDSON: *Assistant*, 1912-'14. [A.B., University of Missouri, 1912.]
- ETHEL WICKWIRE: *Assistant*, 1912-'14. [A.B., Tri-State College, 1909; A.M., Columbia, 1914.]
- TULA L. HARKEY: *Assistant*, 1912-. [A.B., Colorado College, 1909.]
- WILLIAM A. PERLZWEIG: *Assistant*, 1913-. [A.B., Columbia, 1913; A.M., 1914.]
- VICTOR E. LEVINE: *Assistant*, 1913-. [A.B., College of the City of New York, 1909; A.M., Columbia, 1911; Ph.D., 1914.]
- CHARLES WEISMAN: *Assistant*, 1914. [B.S., College of the City of New York, 1900; M.S., New York University, 1902; Ph.D., Columbia, 1913.]
- CHRISTIAN SEIFERT: *Laboratory assistant*, 1898-'14.
- STELLA WALDECK: *Recorder*, 1908-.

## COURSES OFFERED BY THE BIOCHEMICAL DEPARTMENT OF COLUMBIA UNIVERSITY, 1913-'14

(*Abbreviations:* C, conference; D, demonstration; L, lecture; Lw, laboratory work; R, recitation. Odd numbers indicate the first-half, even numbers the second-half, of the academic year; double numerals indicate full academic year. Courses 213-214 and 281-282 are not offered during 1913-'14.)

### ORGANIC CHEMISTRY

51. ELEMENTARY ORGANIC CHEMISTRY. (*Medical School.*) Introductory to course 101 or 102. (*Required of first year students of medicine.*) L, D, R, 2 hr. Lw, 6 hr., each section (2). Profs. Gies and Howe, Dr. Lothrop and Messrs. Knudson and Perlzweig.

### NUTRITION (PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY)

61-62. CHEMISTRY OF NUTRITION. (*School of Pharmacy. Required of candidates for the Degree of Doctor of Pharmacy.*) L, 1 hr. Prof. Gies.

101 or 102. GENERAL BIOLOGICAL (PHYSIOLOGICAL) CHEMISTRY. *A course in the elements of normal nutrition. (Full course.)* Given at the College of Physicians and Surgeons, and at Teachers College.

#### COLLEGE OF PHYSICIANS AND SURGEONS—

*Faculty of Medicine* (primarily): 102—"Nutrition (physiological chemistry) 52." Required of first year medical students. (*Second half year.*)

L, R, D, 2 hr.; Lw, 6 hr., each section (2). Profs. Gies and Howe, Dr. Lothrop and Messrs. Knudson and Perlzweig. (*Also given during the last summer session by Prof. Gies and Messrs. Perlzweig and Levine.*)

*Faculty of Pure Science* (solely): 101—"Biological chemistry 101." (*First half year.*) L, R, 1 hr.; Lw, 7 hr. Prof. Howe, Dr. Eddy and Messrs. Knudson and Perlzweig.

#### TEACHERS COLLEGE—

*School of Practical Arts:* 101 or 102—"Chemistry 51" and "Household Arts Education 125." L, 2 hr.; R, 1 hr., each section (2); Lw, 5 hr., each section (2). (*Each half year.*) Prof. Gies, Dr. Seaman, and Misses Wickwire and Harkey. (*Also given during the last summer session by Prof. Gies, Dr. Seaman and Miss Harkey.*)

201-202. ADVANCED PHYSIOLOGICAL CHEMISTRY, INCLUDING METHODS OF RESEARCH IN NUTRITION. (*Full course. Teachers College, School of Practical Arts.*) L, 1 hr. Lw, 7 hr. Dr. Seaman and Miss Harkey. (This course is designated "Household Arts Education 127" in the Teachers College Announcement.)

204. GENERAL PATHOLOGICAL CHEMISTRY. *Lectures on nutrition in disease. (Teachers College, School of Practical Arts.)* L, 1 hr. Prof. Gies. (This course is designated "Chemistry 52" in the Teachers College Announcement.)

211-212. BIOCHEMICAL METHODS OF RESEARCH, INCLUDING CLINICAL METHODS AND URINARY ANALYSIS IN GENERAL. (*Full course. Medical School.*) L, 1 hr. Lw, 7 hr. Profs. Gies and Howe, Dr. Eddy, and Messrs. Knudson and Perlzweig.

(213-214) CHEMISTRY OF BIOLOGICAL COLLOIDS, ESPECIALLY CARBOHYDRATES, LIPINS, PROTEINS AND ENZYMES. (*Full course. Medical School.*) L, 1 hr. Lw, 7 hr. Prof. Gies.

221-222. NUTRITION IN HEALTH. *A laboratory course in advanced physiological chemistry. (Double course. Medical School.)* L, 2 hr. Lw, 14 hr. Profs. Gies and Howe, and Dr. Morgulis.

223-224. NUTRITION IN DISEASE. *A laboratory course in advanced pathological chemistry. (Double course. Medical School.)* L, 2 hr. Lw, 14 hr. Prof. Gies.

### Courses in Nutrition (continued)

225-226. NUTRITION IN DISEASE. (*Medical School.*) L, 1 hr. Profs. Gies and Howe, and Drs. Mosenthal and Goodridge.

251-252. ADVANCED PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY, INCLUDING ALL PHASES OF NUTRITION. (*Double course. Medical School.*) Research. C, 1 hr. (individual students). Lw, 16 hr. Profs. Gies and Howe, and Dr. Lothrop.

### TOXICOLOGY

261-262. EFFECTS AND DETECTION OF POISONS, INCLUDING FOOD PRESERVATIVES AND ADULTERANTS. (*Full course. Medical School.*) Lw, 6 hr. Prof. Gies.

### BOTANY

271-272. CHEMICAL PHYSIOLOGY OF PLANTS. (*Full course. New York Botanical Garden or Medical School, or both.*) L, 1 hr. Lw, 7 hr. Prof. Gies.

### BACTERIOLOGY

(281-282) CHEMISTRY OF MICROORGANISMS: FERMENTATIONS, PUTREFACTIONS AND THE BEHAVIOR OF ENZYMES. *An introduction to sanitary chemistry.* (*Full course. Medical School.*) L, 1 hr. Lw, 7 hr. Prof. Gies.

### SANITATION

291. SANITARY CHEMISTRY. (*Half course. Teachers College, School of Practical Arts.*) L, 1 hr. Lw, 3 hr. Dr. Seaman and Miss Harkey. (This course is designated "Chemistry 57" and "Household Arts Education 129" in the Teachers College Announcement.)

### BIOCHEMICAL SEMINAR

301-302. BIOCHEMICAL SEMINAR. (*Medical School.*) 2 hr. Prof. Gies.

### RESEARCH IN BIOLOGICAL CHEMISTRY

Biochemical research may be conducted, by advanced workers, independently or under guidance, in any of the departmental laboratories.

### LABORATORIES FOR ADVANCED WORK IN BIOCHEMISTRY

The laboratories in which the advanced work of the biochemical department is conducted are situated at the College of Physicians and Surgeons, Teachers College, New York Botanical Garden and Bellevue Hospital. Each laboratory is well equipped for research in nutrition and all other phases of biological chemistry.

### BIOCHEMICAL LIBRARY

Prof. Gies' library occupies a room adjoining the main biochemical laboratory at the College of Physicians and Surgeons and is accessible, by appointment, to all past and present workers in the Department. The library contains 2600 volumes and 7000 classified separates.

### COLUMBIA UNIVERSITY BIOCHEMICAL ASSOCIATION

The Biochemical Association holds scientific meetings regularly on the first Fridays in December, February and April, and on the first Monday in June. These meetings are open to all who may be interested in them.

### SUMMER SCHOOL COURSES

Courses 101, 225 and 251, or their equivalents, are offered during the summer sessions. Prof. Gies and assistants. See page 520.





The BIOCHEMICAL BULLETIN is a quarterly biochemical review. It publishes results of original investigations in biological chemistry, preliminary reports of investigations, abstracts of papers, addresses, lectures, criticism, reviews, descriptions of new substances, methods and apparatus, practical suggestions, biographical notes, historical summaries, bibliographies, quotations, questions, news items, proceedings of societies, personalia, views on current events in chemical biology, and miscellaneous items of personal and professional interest to chemical biologists.

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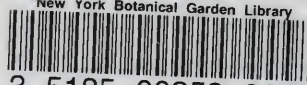








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